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TABLE 2.—Muscle Strength in Disuse Atrophy Cats Following Removal of Cast (Second Study)

Immobilized leg is listed first; control leg, second.

	Cat	Leg	Mean Normal, %	Maximum Deviation from Mean Normal, %	First Week After Cast Removed, %	Second Week After Cast Removed, %	Third Week After Cast Removed, %	Fourth Week After Cast Removed, %	Sixth Week After Cast Removed, %	Eighth Week After Cast Removed, %	Ninth Week After Cast Removed, %
Relaxed	55	R	32.1	6.9	29.0	33.0	35.0	35.0	32.0	Died	
		L	28.5	9.5	37.5	32.5	39.5	33.0	33.0	Died	
	59	L	35.8	1.7	35.0	34.0	36.0	41.0	33.5	34.5	
		R	34.5	5.8	37.5	39.5	33.5	41.5	34.0	33.5	
	69	R	33.3	0.6	29.0	32.0	34.0	32.0	31.5	34.0	
		L	30.7	4.0	26.5	27.5	26.0	35.0	33.5	40.5	
	72	L	41.1	5.1	45.0	35.5	45.5	39.0	40.5	36.5	
		R	38.5	7.0	52.5	45.0	43.0	46.0	36.5	42.5	
	73	L	29.3	3.1	26.5	26.5	29.0	31.5	28.5	27.5	
		R	30.0	4.3	33.0	32.5	34.0	35.5	27.5	30.5	
	76	R	28.1	2.5	29.5	30.5	40.5	35.0	34.5	Died	
		L	33.0	6.1	39.0	36.5	40.0	43.5	38.0	Died	
	77	R	30.0	0.0	16.5	20.5	27.5	27.0	26.5	24.5	
		L	26.2	12.2	26.5	31.5	36.5	35.0	30.0	26.0	
	82	R	33.0	5.2	26.0	30.5	34.0	32.0	32.0	Died	
		L	36.5	8.2	38.0	37.0	41.5	39.0	36.0	Died	
Stretched	62	L	35.1	2.2	24.5	29.5	27.0	28.0	Died		
		R	31.8	5.0	41.5	41.5	37.5	32.0	Died		
	74	R	34.7	7.8	32.0	36.0	37.5	32.0	27.0	27.5	
		L	32.2	7.1	28.0	35.0	31.5	35.0	34.5	31.5	
	75	R	33.7	1.8	29.5	35.0	35.0	33.5	18.5	23.0	
		L	33.3	5.7	32.0	40.0	32.0	36.5	32.0	24.5	
	78	L	35.5	0.0	25.5	27.5	25.0	25.0	26.5	29.0	
		R	39.2	8.4	40.5	41.5	40.5	44.0	45.0	40.0	
	83	R	44.8	4.9	27.5	33.0	32.0	25.5	32.0	29.0	
		L	29.5	6.8	40.5	36.0	35.0	39.5	34.0	30.5	
Neutral	54	R	37.6	2.9	34.0	37.0	35.0	27.0	27.0	....	27.5
		L	36.5	6.8	33.0	36.5	32.5	28.0	34.0	....	26.5
	56	R	37.8	3.4	26.0	31.0	28.5	32.0	30.0	....	32.5
		L	34.8	5.2	39.0	33.5	38.0	37.5	33.5	....	42.5
	84	L	31.3	2.2	41.0	46.5	26.5	26.0	33.0	....	33.5
		R	32.2	11.5	46.0	47.5	41.5	35.0	39.5	....	33.5
	87	R	28.5	5.3	29.0	33.0	30.0	Died			
		L	27.3	8.1	23.5	32.0	27.5	Died			
	88	L	39.5	7.6	42.5	45.5	41.0	41.5	42.5	....	30.0
		R	43.5	11.5	47.5	48.0	49.0	50.0	44.0	....	26.0

TABLE 3.—Significant Variation of Muscle Strength from the Mean Normal Following Cast Removal in Disuse Atrophy Cats (Second Study)

	Cat	Mean Normal Twitch Strength of Immobilized Leg	Maximum Deviation from Mean Normal, %	Actual Maximum Deviation from Mean Normal	Variation in Excess of Maximum Deviation						
					First Week After Cast Removed, %	Second Week After Cast Removed, %	Third Week After Cast Removed, %	Fourth Week After Cast Removed, %	Sixth Week After Cast Removed, %	Eighth Week After Cast Removed, %	Ninth Week After Cast Removed, %
Relaxed	55	32.1	6.9	2.2	-2.8	.....	+2.2	+2.2	.....	Died	
	59	35.8	1.7	0.6	-0.6	-3.4	.....	+12.8	-7.5	-1.2	
	69	33.3	0.6	0.2	-12.4	-3.3	+1.5	-3.3	-4.8	+1.5	
	72	41.1	5.1	2.1	+4.4	-8.5	+5.6	.....	.....	-6.1	
	73	29.3	3.1	0.9	-6.5	-6.5	.....	+4.4	.....	-3.1	
	76	28.1	2.5	0.7	+2.5	+6.0	+41.6	+22.0	+20.3	Died	
	77	30.0	0.0	0.0	-45.0	-31.6	-8.3	-10.0	-11.7	-15.3	
	82	33.0	5.2	1.7	-16.1	-2.4	.....	.....	.....	Died	
				Average	-9.6	-6.2	+5.3	+3.5	-0.5	-5.4	
Stretched	62	35.1	2.2	0.8	-28.9	-13.7	-20.8	-18.0	Died		
	74	34.7	4.9	1.7	-2.9	.....	+3.2	-2.9	-17.3	-15.9	
	75	33.7	1.8	0.6	-10.7	+2.1	+2.1	.....	-43.2	-30.0	
	78	35.5	0.0	0.0	-28.2	-22.6	-29.6	-29.6	-25.3	-15.3	
	83	44.8	3.1	1.4	-35.5	-23.2	-25.4	-17.6	-25.4	-32.2	
				Average	-21.1	-11.5	-14.1	-13.6	-27.5	-24.1	
Neutral	54	37.6	2.9	1.1	-6.6	.....	-4.0	-25.3	-25.3		-23.9
	56	37.8	3.4	1.3	-27.8	-14.6	-21.2	-11.9	-17.2		-10.6
	84	31.3	2.2	0.7	+28.8	+46.4	+14.4	+12.5	+3.2		+4.8
	87	28.5	5.3	1.6	.....	+10.5	.....	Died			
	88	39.5	7.6	3.0	.....	+7.6	.....	.....	.....		-16.5
				Average	-1.1	+10.0	-2.2	-6.1	-9.8		-11.5

..... Indicates variation not in excess of actual maximum deviation.

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removed. This gave time for the muscle to regain its tone, for its circulation to return to an approximately normal condition and for the joints to limber up. We recognize the fact that there was some recovery of power in the muscles during this week but believe that the tests made immediately after the removal of the immobilization are apt to give false impressions, and this is especially true of a muscle which has been immobilized in a position of relaxation.

Further analysis of the data presents several difficulties. The degree of variation of strength from one stimulation to the next in the same animal is unexplained. It is difficult to believe that it is due to a technical error on the part of the operator, since the same technic of stimulation was observed after immobilization as before. The average maximum variation from the mean in at least three stimulations before

sectioning the sciatic nerve at the level of the ischial tuberosity and suturing the two ends back under the muscle so that they were directed away from each other. At the conclusion of the experiment when the gastrocnemius muscles were dissected free and weighed, the area of nerve section was carefully inspected and no evidence of union found in any of the animals, the ends of the nerve being in most cases  $\frac{1}{2}$  to  $\frac{3}{4}$  inch (1.2 to 1.9 cm.) apart.

Twelve of these animals were denervated and not immobilized. These controls were stimulated once a week in order to determine the normal course of atrophy measured by our apparatus. Nine of the animals were followed for six weeks or more and 6 of them for as long as ten weeks. The other 12 animals were denervated and immobilized immediately for a period of six weeks, 6 in the stretched and 6 in the relaxed position. Another 6 would have been immobilized in the neutral position, but the control group had shown our method to be unreliable for stimulation of denervated muscle.

Denervation of muscle increases the time-strength characteristic (chronaxia), as shown by

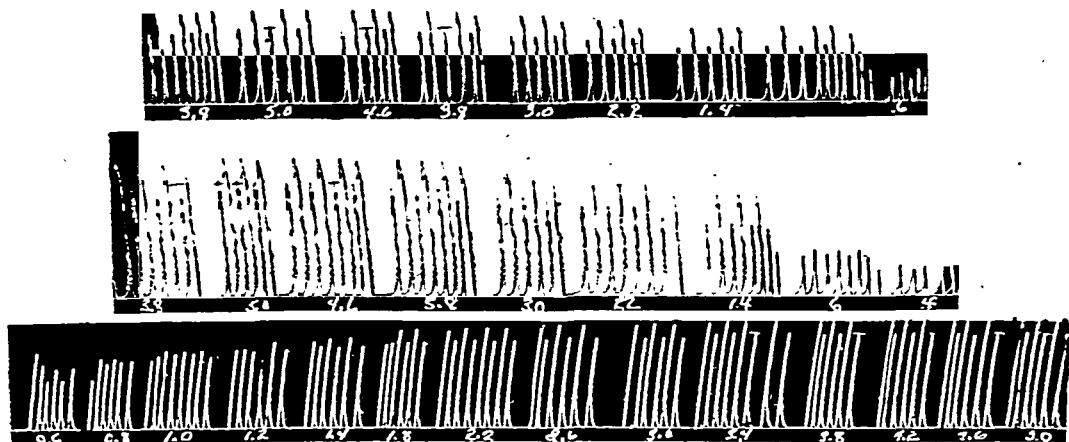


Fig. 5.—Record of twitch height in denervated muscles. Upper and middle records show no plateau. Lower record shows plateau from 3.4 to 5 amperes. Plateau height denoted by compass marks. Stimulation amperages listed below each group.

immobilization was only 4 per cent in this group and, as stated before, in a total of 51 cats not more than 4.6 per cent. Furthermore, it is peculiar that in 3 cats the muscles showed an increase in strength following immobilization.

## OBSERVATIONS ON DENERVATED MUSCLES

The studies on denervation were carried out with the idea of determining whether immobilization had any effect in delaying or lessening the atrophy of denervation and, if so, which position was the most effective.

In 24 cats the mean normal twitch in the strength of muscles was determined by at least three stimulations one week apart, and for an animal to be used the maximum deviation from the mean had to be less than 10 per cent. The leg which showed the least deviation from the mean was chosen for denervation. This was carried out by

Adrian<sup>11</sup> (1916). Therefore the denervated legs were stimulated with only 20,000 and 30,000 ohms in the secondary, thus producing a longer-acting stimulus. Still no definite plateau could be obtained consistently. Sometimes a plateau from 3.8 to 5 amperes could be recorded, while at other times no plateau could be found even up to 5 amperes (fig. 5). This applied to stimulation of an individual muscle from week to week as well as to the group as a whole. We attributed this inability to obtain a plateau in the denervated muscles to several factors. With denervated muscle, excitation is entirely through the muscle fibers and, in contrast to the disuse atrophy muscles, no nerve stimulation occurs.

11. Adrian, E. D.: The Electrical Reaction of Muscles Before and After Nerve Injury. *Brain* **39**:1-33, 1916.



## ENTRICULOGRAPHIC DIAGNOSIS OF STRICTURE OF THE AQUEDUCT

The positive diagnosis of a stricture can now usually (not always) be made by a study of the shape of the air shadow at the obstruction as disclosed by ventriculography. The ventricular system ahead of the obstruction must be completely filled with air to insure filling of the third ventricle and of the aqueduct if it is patent.

Less than complete filling leads to uncertainty and frequently to error in interpretation. The air shadow is frequently pathognomonic of a stricture. From a somewhat dilated, or possibly normal-sized, opening of the aqueduct in the third ventricle, the air shadow tapers backward to a point in the midbrain—i. e., the shadow is

ever, is uncommon. It will be understood, of course, that a stricture of the aqueduct always dilates the entire ventricular system ahead of the aqueduct, and it is then necessary only to concentrate the inspection of the ventricular shadows to the point of obstruction. It will also be observed that the hydrocephalus due to a stricture of the iter is frequently much greater than that caused by tumors in the posterior fossa, because in the latter the obstruction is intermittent and of ball valve character until the final stages. It is probable that for years after birth there is a tiny lumen in an aqueduct with a stricture and that eventually it closes completely. That is the only plausible explanation for the appearance of the strictures in late childhood and even beyond.

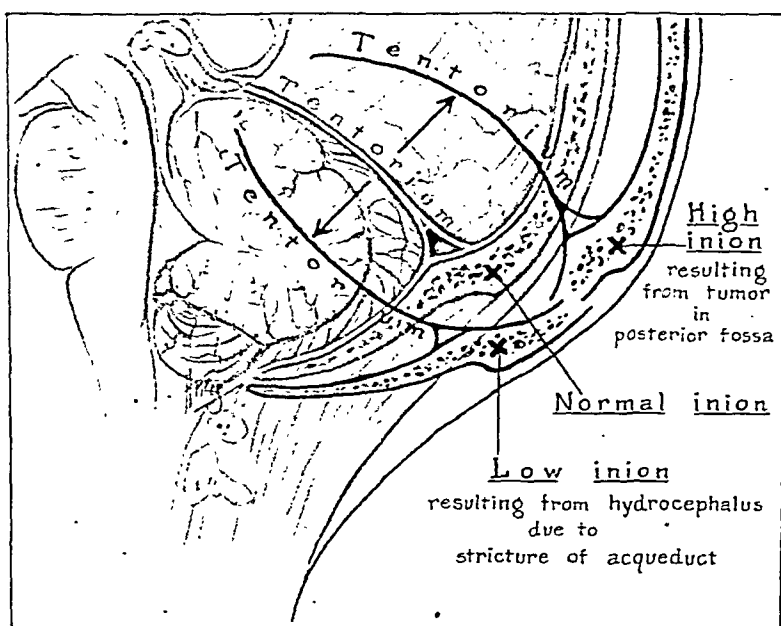


Fig. 4.—Diagram to show the shifting of the height of the inion (1) upward, by a tumor in the posterior fossa, and (2) downward, by a supratentorial pressure of hydrocephalus.

funnel shaped or triangular (figs. 1 and 2). The shape of the shadow is determined, of course, by the character of the lesion, i. e., a scar which gradually becomes more intense as it passes backward. Usually when this lesion is present, the entire length of the open aqueduct is less than 0.5 cm. Such a shadow differs from that of an obstruction by a tumor in that the latter causes a sudden obstruction and therefore a sharp vertical line at the point of obstruction and the part of the aqueduct anterior to it is uniformly dilated, because there is no scar to constrict it. Occasionally a diaphragmatic obstruction of the aqueduct exists, and when this obtains the roentgenographic shadow is precisely like that of a tumor; such an obstruction, how-

However, in none of the patients who have been operated on in this hospital has any air been found beyond the aqueduct; i. e., the strictures were then probably complete.

## DIAGNOSIS OF STRICTURES OF THE AQUEDUCT WITHOUT VENTRICULOGRAPHY, I. E., BY THE HEIGHT OF THE INION

It is now possible to make the diagnosis of stricture of the aqueduct without operation and even without ventriculography. This had been done in 5 cases. The clue to the diagnosis is the height of the inion. Roentgenologic examination is usually a better guide to the site of the inion than palpation, because the inion may be difficult to feel with accuracy. Also, the lateral venous

be done with relative safety. We further believe that when practical internal fixation should be used for fractures complicated by nerve lesions in order that external fixation may be reduced to a minimum. For this, there may be a place for the dual plates recently described by one of us (J. A. K.).

During the course of the work, we have thought of several means to improve the method and to eliminate obstacles which were encountered. Since we cannot effect them at this time, we make them as suggestions to any one interested in carrying this work further.

1. In denervated muscle, a satisfactory plateau could probably be obtained on stimulation if smaller experimental animals were used. The main factor in our inability to obtain this plateau was the size of the muscle which was so great in cats that stimulation of all the muscle fibers required current strengths which stimulated the fibers nearest the electrodes more than once. The smaller the muscle mass, the less important this factor would be.

2. Arcing across the points of the hand switch was another difficulty. A thyrotron would eliminate this, give better control of stimulating currents and make possible their use at much higher values acting for a shorter time. It could also be set to deliver a standard number of stimuli at each current strength used, thus eliminating excess stimulation and any fatigue factor which that may introduce.

3. The twitch measures immediate power but gives no indication of endurance. A study of tetanic strength in disuse and denervation atrophy may yield important information. Such a study was not possible with our apparatus because the inductorium could not carry the necessary current strength. A thyrotron, however, would provide a means for constant strength tetanic stimulation at high currents.

#### SUMMARY

This study attempts to determine two things: (1) the optimum position of fixation of limbs in order to conserve muscle power and (2) the

best method of treatment of muscles paralyzed by loss of nerve supply.

A review of the literature on muscle physiology shows that in most of the studies of disuse and denervation atrophy weight has been used as a criterion of the atrophy. Functional studies have employed methods requiring the killing of the animal after one stimulation. Only one functional study has been reported in which the same animal was repeatedly stimulated, and this method was not satisfactory for our purpose.

A method was developed for recording the twitch strength of the gastrocnemius-soleus group of muscles in cats. By means of the described method, animals have been stimulated as much as twelve different times without noticeable ill effect.

In a series of 51 normal cats stimulated at weekly intervals, this method yielded normal values for one leg, which showed only 4.6 per cent average maximum deviation from the mean, with a maximum deviation range of 0 to 8.3 per cent.

This method was applied to the study of disuse atrophy. After normal values were determined legs were immobilized for six weeks, with the muscle group in stretched, relaxed and neutral positions. Stimulation for eight weeks following removal of the cast showed moderate and persistent disuse atrophy in the muscles which were stretched, whereas the relaxed and neutral groups showed little consistent effect.

Denervated cats also were immobilized in various positions, but the study was unsatisfactory because no definite contraction plateau could be obtained in response to stimulation.

On the basis of the data obtained from denervated cats, however, the suggestion is made that denervated muscles atrophy less if left alone than if immobilized. Emphasis is also placed on repairing the nerve before the bone is healed when fractures are complicated by peripheral nerve injuries.

Dr. George Bishop, Professor of Biophysics, Washington University School of Medicine, has given help, without which this method could not have been developed.

Clarence E. Rupe, M.D., has given technical assistance in some of these experiments.

ice in this series of cases, once in an infant and once in an adult. In the latter case, the anterior approach was tried subsequently, but without success. It should be noted that in children and adults the floor of the ventricle is always thicker than in infants, and, to prevent subsequent closure, a larger opening is required. In 7 cases in

group I, the opening had closed after a short time, but after a second and in 1 case a third operation on the same or the other side the opening has persisted permanently.

A third ventriculostomy is also indicated in some cases of inoperable tumor of the cerebellum, in which there are no crippling sequelae of

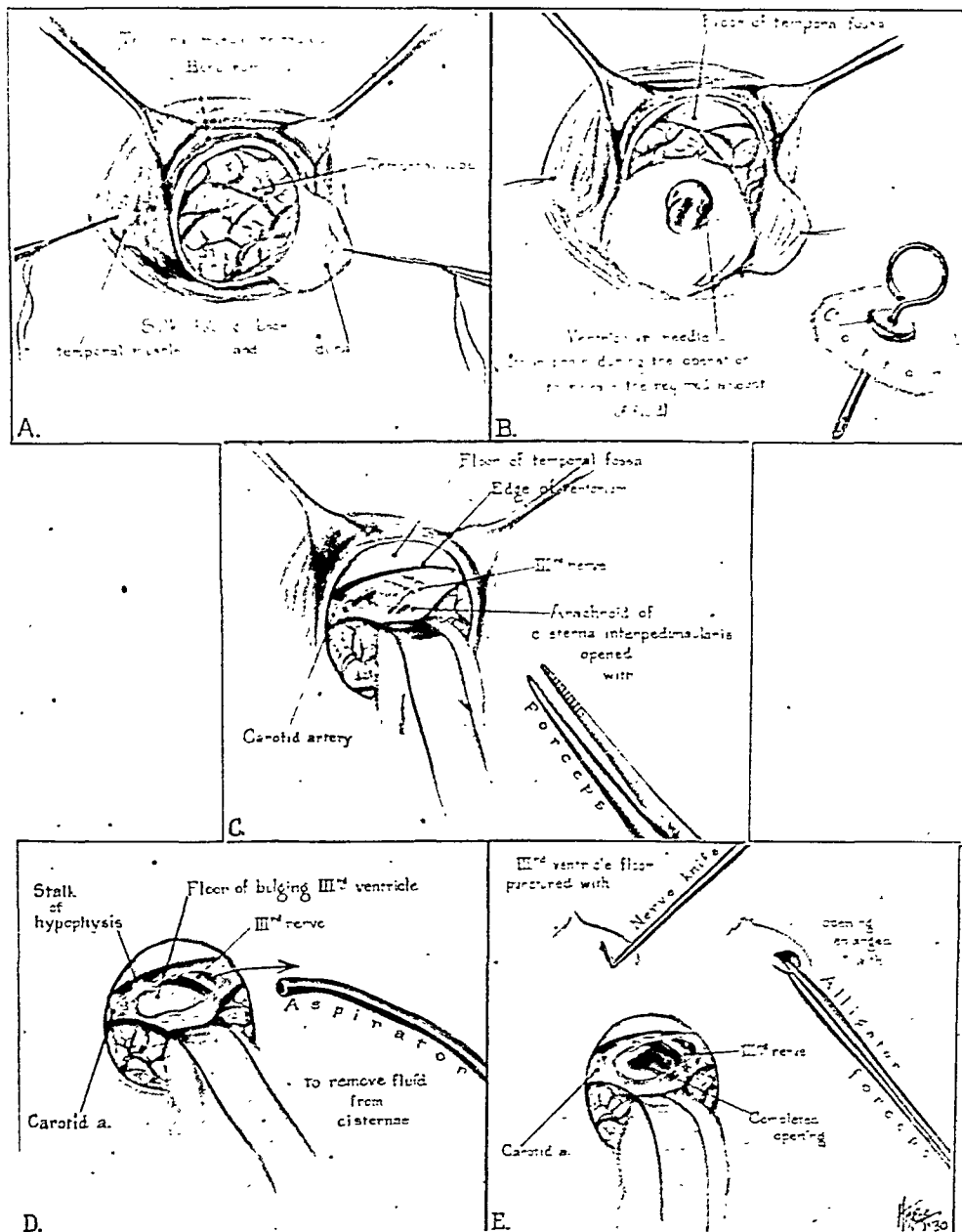


Fig. 7.—Drawing to demonstrate the steps in the procedure of third ventriculostomy by the lateral or temporal route: *A*, exposed brain. *B*, a flanged needle protected by a pledget of cotton is passed into the descending horn and left in place during the operation. Fluid rolls out in the exact amount required to gain room when the spatula elevates the temporal lobe. *C*, exposure of the cisterna interpeduncularis; the third nerve shines through the membrane. *D*, the floor of the ventricle can be seen bulging into the cisterna interpeduncularis, the wall of which is removed. *E*, opening made into the floor of the ventricle by plunging the forceps into it or by cutting it with a knife or scissors. The opening can be enlarged by spreading the forceps, by pulling the thin ventricular wall or by cutting it with angle scissors.

cast prior to operation to which group any given patient will ultimately belong" and, consequently, advocated maintenance of the external secretory function of the pancreas. Further support to the importance of preserving the pancreatic juice has been given recently by Whipple.<sup>5</sup>

When one has adopted the idea that some variety of pancreaticoenterostomy is desirable, the problem arises of developing a satisfactory technic. Experimentally, several methods have been applied, beginning in 1909 with the complicated procedure of Coffey.<sup>6</sup> In 1915 Sweet and Simons<sup>7</sup> described a method of implantation of the divided pancreatic stump of a dog into the small intestine, while Patrie, Pyle and Vale<sup>8</sup> in 1917 reported a similar procedure on dogs, with a satisfactory functional result. More recently, Person and Glenn<sup>9</sup> demonstrated the feasibility of implanting the pancreatic stump into the stomach by open anastomosis in dogs. Their results indicated that pancreaticogastrostomy produces a normally functioning fistula and that in such a situation atrophy of the pancreas, acute pancreatitis, peritonitis and deposition of lipids in the liver do not occur. Extending the matter of pancreaticoenterostomy further, Poth,<sup>10</sup> Child<sup>4</sup> and Cattell<sup>2k</sup> each have applied some form of the procedure in clinical practice, with satisfactory results.

An evaluation of the technics employed by the aforementioned investigators directs attention to two important factors: with the exception of Cattell's<sup>2k</sup> simple method, all procedures involve an open anastomosis, thereby causing a breach in asepsis, and most are too time consuming, even though mechanically simple. The radical operative treatment of periampullary and pancreatic carcinoma is a formidable test of the patient's endurance, and the conservation of time may be an important factor in the ultimate outcome. Inasmuch as the disposal of the pancreatic stump represents a terminal step in the

procedure, when the patient's vitality is lowest, the method of managing this technical detail should be uncomplicated and quickly performed. As regards asepsis, it is advisable to avoid, if possible, opening the intestine in the presence of the large raw surface created by duodenectomy. With the idea in mind of developing an aseptic technic which can be performed with minimal loss of time and by which the external pancreatic secretions can be preserved, the following experimental study was conducted.

#### METHOD

Twenty-two dogs were studied. Fifteen were subjected to operation under anesthesia induced by intravenous injections of pentobarbital sodium by the following technic. The duodenum was delivered into the wound along with the attached pancreas. The gland was divided at the junction of the uncinate process and the body without disturbing the relationships of the latter to the duodenum (fig. 1A), thereby leaving intact the junction of the main pancreatic duct with the ampulla of Vater. The exposed transected surface of pancreatic body was closed by interrupted invaginating sutures of fine silk after ligation of the divided duct (fig. 1A). In this manner, the long uncinate process (10 to 15 cm.) was isolated entirely from the remainder of the gland, maintaining its independent blood supply intact. No attempt was made to ligate the divided end of the uncinate duct, but it was allowed to retract into the parenchyma of the gland (fig. 1B). A loop of jejunum about 7 inches (17.7 cm.) from the ligament of Treitz was next brought into the wound. In the long axis of the antimesenteric surface of the jejunal loop, an incision was made of sufficient length to accommodate the cut surface of the uncinate stump. Particular care was taken to carry the incision down to, but not through, the mucosa, so that an opening into the lumen would not occur. The serosal edges of the incision were spread apart gently, and the stump of the divided uncinate process, with its retracted duct, was implanted into the jejunal wall and made secure by interrupted sutures of fine surgical gut (fig. 1C). The abdominal wound was closed in layers.

The remaining 7 animals were operated on by a modification of the technic of Cattell.<sup>2k</sup> The procedure was similar in detail to that described, except that the uncinate duct was isolated and dissected free from its surrounding parenchyma so as to protrude from the divided stump of the gland. A crushing ligature of fine surgical gut was tied tightly about the protruding duct. One end of the ligature was then passed as a suture through the exposed jejunal submucosa and tied firmly to the other end, thus bringing the crushed duct against the mucosa in a firm, necrotizing ligature (fig. 1D). The pancreatic stump was secured into the jejunal wall in the usual manner (fig. 1C).

All animals survived and remained in good condition. Each was fed the same diet of prepared commercial dog food containing relatively low concentrations of protein and fat. No particular effort was made to supply pancreatic secretagogues.

Observations of the state of the pancreaticoenterostomy were made at intervals varying from seven to forty-eight days by the following technic. The abdomen of each dog was reopened, with the animal under anesthesia induced by intravenous injections of pentobarbital sodium, and the pancreaticoenterostomy exposed. The

5. Whipple, A. O., in discussion on Dragstedt, L. R.: Some Physiologic Problems in Surgery of the Pancreas, *Ann. Surg.* **118**:591, 1943.

6. Coffey, R. C.: Pancreatic-Enterostomy and Pancreatectomy: A Preliminary Report, *Ann. Surg.* **50**: 1238, 1909.

7. Sweet, J. E., and Simons, I. H.: Some Experiments on the Surgery of the Pancreas, *Ann. Surg.* **61**: 308, 1915.

8. Patrie, H. H.; Pyle, L. A., and Vale, C. F.: Recent Experimental Studies of the Pancreas, *Surg., Gynec. & Obst.* **24**:479, 1917.

9. Person, E. C., Jr., and Glenn, F.: Pancreaticogastrostomy, *Arch. Surg.* **39**:530 (Oct.) 1939.

10. Poth, E. J.: The Implantation of the Pancreatic Duct into the Gastrointestinal Tract, *Surgery* **15**:693, 1944.

sion) is proof of the patency or nonpatency of the newly created opening. The decompression should be flat and soft if the hydrocephalus has been cured.

There was 1 operative death in the series. In 1 case (age 17) it was not possible to make an opening in the third ventricle because it did not descend far enough. An anterior approach was tried; the optic nerve was cut to reach it, but the opening was small and quickly closed again. The patient died four months later. Three other patients died at home five weeks, six months and six months after leaving the hospital. In none of these cases was an autopsy obtained; one of these patients had made great improvement; in one there was no improvement, and in no comment was made concerning the third.

remaining patients are well, active and normal mentally and physically.

There are probably no groups of patients with a background of intracranial pressure that do better than those with stricture of the aqueduct and in which the procedure is so simple and safe. The earlier the diagnosis is made, the better the operative results will be.

*Group II (Under 1 year).*—The operative cures obtained in group II are far less than in the preceding one, i. e., in patients over 1 year of age. In the first place, the failures of the operation to sidetrack the fluid into the subarachnoid space are approximately one half, whereas for the patients over 1 year of age failures are very uncommon. The reason for this difference is not



Fig. 12.—*A*, photograph of a patient at the age of 8½ months, showing a marked degree of hydrocephalus. The head then measured 52.5 cm. *B*, the same patient at the present time, twelve years later. The head does not look much oversize, but according to the mother's measurements it is 62.5 cm. in circumference. This may be a mistake, or at least it must include a good deal of hair, because the head does not look so large. The patient is perfectly well.

From the series, 24 are living and cured (figs. 9, 10 and 11). The time since operations was: between six months and one year, 2 cases; between five and ten years, 11 cases; between ten and twenty years, 3 cases, and in 1 case twenty-three and one-half years (fig. 14). Four were mentally retarded in degrees; 1 goes to school but makes little progress; another is in high school but has difficulty keeping up with his classes; the other 2 are morons.

Three patients have greatly defective vision but can see. The vision is not worse than before the operation and in 1 instance has improved a little.

Aside from these defects, which are caused by the long-sustained intracranial pressure, the

too clear, and the explanation offered may or may not be correct. It is my impression that the subarachnoid spaces leading from the cisterna interpeduncularis over the cerebral hemispheres may be compressed over such a long period that they may not reopen. In several instances air has been injected intraspinally before operation, and the air has reached but not passed beyond the cisterna interpeduncularis. Since the hydrocephalus in these patients was doubtless present in intrauterine life, these spaces may never have been open and functioning. Consequently, it may be expecting too much to anticipate their reestablishment with uniformity after they have been obliterated for so long. At any rate, these spaces do open in some cases, and when this

## RESULTS

None of the animals showed gross evidence of active peritonitis or fat necrosis, although local adhesions about the pancreaticoenterostomy were pronounced in 4 (18 per cent) and moderate in 11 (50 per cent); in the remaining 7 (32 per cent), adhesions were slight or absent. Other significant observations are summarized in the table.

*Response to Secretin.*—Of the 22 animals studied, 15 showed definite secretion of pan-

Among the 6 remaining failures, dogs 4, 5 and 12 were tested within nine days of the operation. Despite the negative response of dogs 4 and 5, microscopic sections showed that a junction had been made between the pancreatic duct and the jejunal mucosa, while dog 12 showed acute pancreatitis and no evidence of fistula. Two other negative responses occurred, in dogs 7 and 8, investigated at twenty-one and twenty-six days respectively. Microscopic sections in these animals revealed diffuse fibrosis of the pancreatic

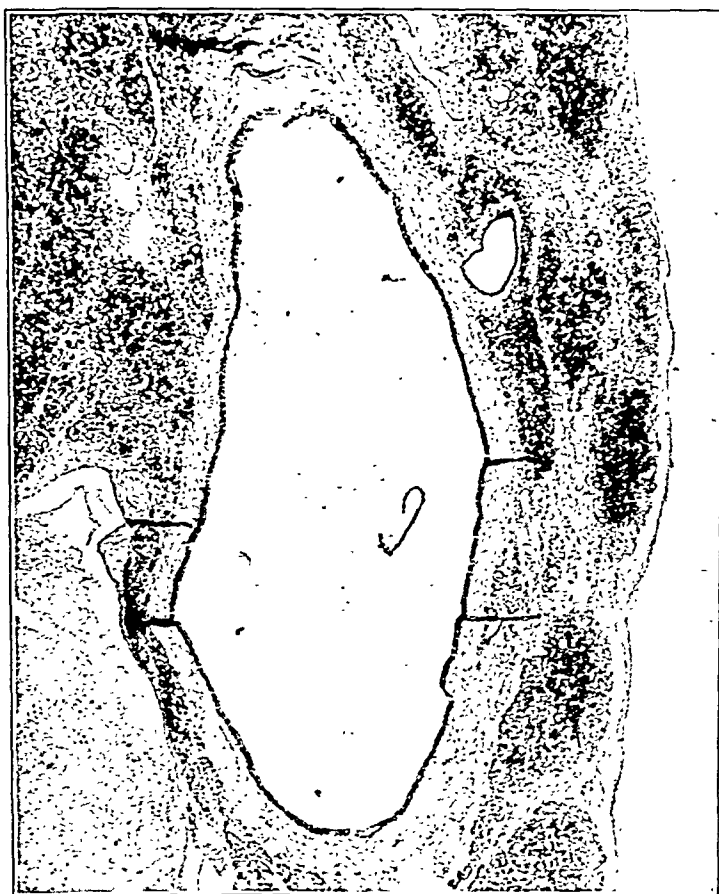


Fig. 2.—Pronounced dilatation of the duct due to obstruction from fibrosis. Note the flattened epithelial lining and the moderate degree of parenchymal scarring ( $\times 40$ ).

creatic juice at the pancreaticojejunal junction after intravenous injection of secretin, an incidence of spontaneous fistula formation of 68 per cent. One (dog 11) died of air embolism immediately after the injection of secretin into the vena cava, so that no determination of the secretory response could be made. Elimination of this animal from the series would result in an incidence of 71 per cent of spontaneous fistula formation.

stump, failure of the duct to form a junction with the jejunal mucosa and pronounced dilatation of the duct system (fig. 2). In the last failure, dog 9, a large retention cyst of the implanted stump developed, containing fluid which gave a strongly positive reaction for amylase.

*Acute Pancreatitis.*—Microscopic studies of the implanted pancreatic stumps revealed some evidence of acute inflammatory reaction in 6 animals; an incidence of 27 per cent. As noted in the table, pronounced diffuse pancreatitis was

# CHRONIC SCLEROSING PANCREATITIS CAUSING COMPLETE STENOSIS OF THE COMMON BILE DUCT

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All surgeons are familiar with acute pancreatitis of the edematous and necrotic types which are associated with relatively fulminating manifestations but associated with only slight or no obstruction of the common bile duct. They are likewise familiar with temporary complete obstruction of the common duct caused by localized chronic pancreatitis involving the head of the pancreas. These lesions are usually localized to the head of the pancreas and are so hard and nodular that it is difficult to differentiate them from carcinoma. Fortunately, this type of localized pancreatitis usually subsides within a few months and thus allows restoration of patency of the common duct. In this presentation we wish to call attention particularly to the other type of chronic pancreatitis, namely, that associated with diffuse atrophy and fibrosis throughout the entire gland. Such a process may produce surprisingly little physiologic or mechanical disturbance. However, on other occasions jaundice may develop and become permanent because of the severity of the sclerosing process involving the common duct. Fortunately, this condition is not common. However, the seriousness of obstruction of the terminal end of the common duct by the progressive pancreatitis is sufficiently well appreciated that every effort should be made to treat acute pancreatitis early and eliminate it if possible. We have encountered 3 patients with a prolonged obstruction of the common duct produced by chronic fibrosing pancreatitis; the clinical observations and methods of therapy in their cases are discussed later.

Riedel<sup>1</sup> in 1896 was the first to associate chronic, benign, inflammatory lesions of the pancreas with obstructive jaundice. In 1900 and again in a monograph in 1907, Mayo-Robson<sup>2</sup>

emphasized the clinical similarity of chronic pancreatitis localized to the head of the pancreas to carcinoma of the pancreas.

A case reported by Carter<sup>3</sup> in 1935 may have been an example of permanent obstruction of the common duct by pancreatitis, but in his case the obstruction had been present only five weeks previous to operation. Yet at autopsy (the patient died of pneumonia) the gland substance was found to be replaced by fibrous tissue in the area surrounding the common bile duct and the common bile duct showed pronounced fibrosis of the wall with narrowing of its lumen, although it retained a normal mucous membrane.

The relative infrequency of stenosis of the common duct secondary to chronic sclerosing pancreatitis is illustrated by the fact that in a review of 80 consecutive cases of stricture of the common duct, Walters<sup>4</sup> did not encounter any in which the stricture was produced primarily by pancreatitis, although in 1 it was secondary to a calcified pancreatic cyst. In 77 of his series, the obstruction had occurred after operation on the gallbladder or bile ducts. Although not all of these were traumatic in origin, enough were to impress one with the extreme seriousness of accidental injury to the common duct.

The etiologic factor in the production of the usual type of acute edematous pancreatitis appears to be strongly related to cholelithiasis; the fact that in most cases the pancreatitis subsides after cholecystectomy is suggestive proof of this relationship, but it is by no means conclusive, since not infrequently cholecystectomy fails to stop the pancreatitis. Occasionally it develops after cholecystectomy. Reference has already been made to the fact that localized pancreatitis in the head of the pancreas, simulating carcinoma, is rather commonly observed by surgeons. For-

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1. Riedel: Ueber entzündliche der Rückbildung der Vergrößerungen des Pankreaskopfes, *Berl. klin. Wchnschr.* 33:1 and 32, 1896.

2. Robson, A. W. M.: On Pancreatitis with Especial Reference to Chronic Pancreatitis, Its Simulation of Cancer of the Pancreas and Its Treatment by Opera-

tion, with Illustrative Cases, *Lancet* 2:235-240, 1900; Pancreatitis Due to Direct Extension of a Malignant Growth of the Gallbladder Along the Common Bile Duct and Pancreatic Ducts, *ibid.* 2:508-511, 1907.

3. Carter, R. F.: Benign Fibrous Stenosis of the Common Duct, *Am. J. Surg.* 30:110-114 (Oct.) 1935.

4. Walters, W.: Strictures and Injuries of Bile Ducts, *J. A. M. A.* 113:209-213 (July 15) 1939.

of pronounced diffuse acute pancreatitis unaccompanied by fat necrosis. This factor, in association with the short postoperative interval, was considered sufficient explanation for failure of secretion to occur. The other failures were dogs 7, 8 and 9, all killed three weeks or more after operation. The first 2 showed moderate diffuse fibrosis with considerable dilatation of the duct (fig. 2), and no evidence of pancreatitis, indicating that obstruction of the duct resulted from fibrosis of the adjacent parenchyma. In dog 9 a large retention cyst developed which replaced the entire uncinata parenchyma, owing to failure of the duct to break through the jejunal wall. Studies of the excised specimens of dogs 7, 8 and 9 failed to reveal any explanation of the selective action of fibrous tissue in causing obstruction of the ducts. Furthermore, it could not be determined from the investigations what factors decided whether cyst formation or simple dilatation would occur.

Varying degrees of acute pancreatitis occurred in 6 animals. Two of these showed evidence of slight patchy inflammation, principally around the sutures; 2, moderate diffuse reactions which did not interfere with secretion and 2, extreme diffuse inflammatory infiltration. In those animals in which the uncinata duct was allowed to retract into the parenchyma of the gland, a collection of pancreatic juice might be expected to develop at the site of implantation, pending spontaneous breakthrough into the jejunum, in a high percentage of instances. In such circumstances, diffuse pancreatic necrosis would be inevitable in a considerable number of cases. The development of slight, patchy, acute pancreatitis in 2 dogs and moderate diffuse pancreatitis in 2 is evidence that such a situation does not occur frequently. On the other hand, a crushing ligature about the duct, holding it firmly against the jejunal submucosa, should minimize the local accumulation of pancreatic secretion and thereby eliminate the subsequent development of diffuse pancreatitis. Actually, the only 2 instances of severe pancreatitis occurred in animals subjected to the latter technic. The first was found in dog 12, investigated seven days after operation and showing a negative response to secretin. The second was found in dog 21, thirty-four days postoperatively, in which the reaction to secretin was positive. In the latter animal, the pancreatitis was acute and the fibrosis was minimal, indicating that the inflammatory process developed late in the postoperative course. The interesting aspects of this case pertain to the pathogenesis of the pancreatitis and to the possibilities of its late effects had the animal been allowed to live longer. At the

time the dog was killed, there was no obvious condition to suggest a disease of any kind.

Despite the fact that 15 dogs presented no evidence of acute pancreatitis, some degree of fibrosis was noted in all but 2 of the total number. This situation may be interpreted as meaning that at some period of the postoperative course inflammatory infiltration of the implanted stump occurred, being displaced by scar tissue at a later date. If this reasoning is correct, it is suggested that acute pancreatitis develops shortly after operation in the majority of animals, is limited in its scope and is successfully replaced by fibrous tissue proliferation. An important observation is the fact that of 18 animals showing varying degrees of fibrosis of the stump (omitting dogs 5, 9, 11 and 20; see the table), only 4 showed a negative response to secretin. It is significant that considerable amounts of acinar tissue can be replaced by scar without eliminating the secretory function of the gland (fig. 4). Apparently, as noted in dogs 7, 8 and 9 (see the preceding section), scarification interferes with function only when it causes obstruction of the duct. There are no possible means of predicting this selective action before pancreaticojejunostomy is performed, but its incidence is low in the animals studied in this series.

#### SUMMARY AND CONCLUSIONS

An aseptic technic of implanting the transected uncinata process of the dog's pancreas into the wall of the jejunum is described.

Spontaneous fistula formation developed between the divided pancreatic stump and the jejunum in 71 per cent of the animals, as determined by the appearance of pancreatic juice at the fistula after intravenous injection of secretin.

A low incidence of the usual complications of transection of the pancreas occurred, there being no peritonitis, no external pancreatic fistula, 1 retention cyst and 2 instances of severe acute pancreatitis.

All animals survived and remained in good health regardless of whether complicating factors developed or whether pancreaticojejunal fistulas were formed.

A significant fact noted was that fibrous tissue infiltration of the implanted pancreatic stump can occur to a considerable extent without interfering with the secretory function of the gland.

Results obtained in this study suggest application of the methods described to patients undergoing radical surgical treatment of carcinoma involving the head of the pancreas and the periampullary region, for whom preservation of the external secretion of the pancreas is desired.



15, 1943, a chronically diseased gallbladder was removed and a gallstone 1 cm. in diameter was removed from the common bile duct. The pancreas was removed one and one-half times and was indurated and nodular. The patient's postoperative period was stormy because of excessive and prolonged vomiting and loss of appetite. He was discharged from the hospital with the T tube in place. Clamping of the tube daily for several hours was well tolerated, and it was removed on the eighteenth postoperative day.

However, removal of the tube was followed in twenty-four hours by cramping epigastric pain, nausea, vomiting and a temperature of 100.6 F. He was again admitted to the hospital (one month following cholecystectomy) with a white blood cell count of 12,000 and an icterus index of 40. These findings, together with pain and tenderness transversely in the epigastrium, made a diagnosis of subacute or acute pancreatitis obvious; it was thought that a mild suppurative cholangitis perhaps accompanied the pancreatitis, but infection was not severe enough to warrant drainage by operation. The patient responded well to con-

All manifestations, including jaundice and fever, subsided within a few days following drainage of the common duct. However, during a period of two months' observation, the stools remained acholic. At the end of this time (Dec. 20, 1943), a laparotomy was performed with the idea of anastomosing the common duct to the duodenum. This was accordingly done. A complete stenosis of the terminal portion of the common duct was found; the pancreas was hard, nodular, atrophic and about half the size of a normal pancreas. For reasons to be discussed, a transduodenal choledochoduodenostomy was then done, as illustrated in figure 4. This was one of those occasions (fortunately rather uncommon) when removal of a diseased gallbladder failed to relieve an accompanying pancreatitis.

Although this patient had pancreatitis at the first operation, it was thought that the obstruction of the common duct which he had had for two months prior to his initial entrance into the hospital was due to the stone in the common duct. Regardless of the cause of the obstruction, he had a slow recovery for a few weeks because of persistence of the obstruction, but he did recover and remained free of symptoms for several weeks. The obstruction preceding his third, and last, operation was complete but only of two months' duration. Since it was of such short duration, it is perhaps not accurate to consider this as a permanent obstruction, but the fibrosis in the region of the head of the pancreas was so dense and accompanied with so little edema that recovery of patency of the common duct appeared entirely unlikely.

#### THERAPY

Complete permanent obstruction of the common duct due to chronic pancreatitis is a difficult lesion to treat but much less difficult than obstruction due to complete absence or destruction of the common duct, because the remnant of common duct simplifies the operative procedures. When the obstruction is due to localized pancreatitis involving only the head of the pancreas, the prognosis for spontaneous complete recovery appears to be much better than when a generalized chronic sclerosing pancreatitis is producing a complete obstruction of more than transient type. Therefore, the customary operation of cholecystenterostomy for local pancreatitis in the head of the pancreas appears to be a logical procedure, particularly since, in our opinion at least, the anastomosis will frequently remain open for only a few months, at the end of which time the pancreatitis usually subsides completely with relief of the obstruction. The operation of cholecystenterostomy has one serious disadvantage—namely, development of cholecystitis and hepatitis as has been shown experimentally by Wangenstein<sup>5</sup> and others. Food is bound to collect in the gallbladder unless a type of anastomosis similar to that performed in case 2 (see figure 3) is performed.

5. Wangenstein, O. H.: Cholangitis Following Cholecystenterostomy, *Ann. Surg.* 87:54-65 (Jan.) 1928.

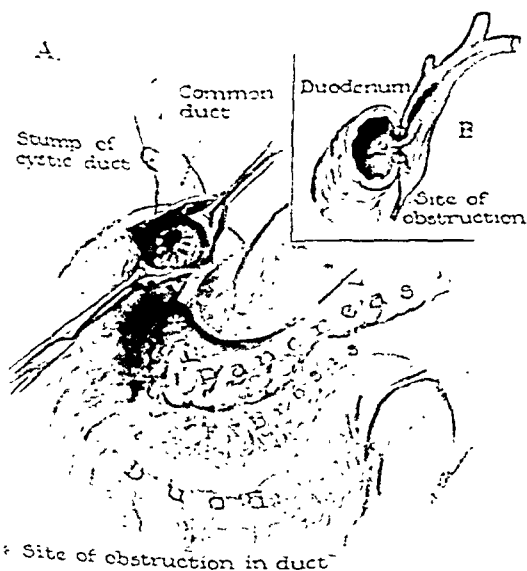


Fig. 4.—A transduodenal anastomosis was performed in this patient because we had already opened the duodenum to inspect the sphincter of Oddi and because we found that the duct was firmly adherent to the duodenum at the point where the anastomosis was made. Actually no sutures would have been necessary, but two or three were taken to maintain fixation in case the adherence of the wall of the duct to the duodenal wall was not solid.

ervative supportive measures and in four days was discharged. He had no complaints then until five months later, when he had a rather sudden onset of epigastric pain radiating to his back, associated with nausea, vomiting, fever and jaundice. After several days in the hospital, with progression of the symptoms, it became evident that the patient was suffering from rather severe suppurative cholangitis superimposed on the obstruction of the common duct which had again returned. Operation was performed and the common bile duct drained. The pancreas was still indurated and nodular but smaller than at the first operation. At this time it was impossible to pass a probe into the duodenum through the sphincter of Oddi.

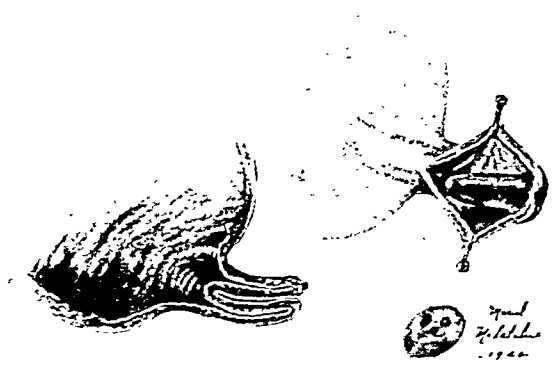
into the ascending colon. If the intussusception becomes compound, then the clinical picture is that of intestinal obstruction.

The treatment of intussusception of the appendix into itself is appendectomy. In the event of a completely intussuscepted appendix, the appendix is removed by resecting a small cuff of cecum which surrounds the base of the appendix. The compound variety may be easily reduced, but if gangrenous, resection of a portion of the cecum and anastomosis of the ileum to the ascending or transverse colon are required.

#### REPORT OF A CASE

A 45 year old bipara was seen by a physician three years prior to operation for severe pain of twelve hours' duration in the right lower quadrant. The sudden acute pain was associated with nausea, vomiting and abdominal tenderness. Physical examination demonstrated tenderness without spasm in the right lower quadrant, a normal uterus and normal vaults. Her white blood cell count was 22,500, blood pressure 96 systolic and 60 diastolic and pulse rate 64. The urine was normal. Her pain and tenderness subsided in forty-eight hours, and she was well until one month later, when a similar pain in the right lower quadrant of the abdomen occurred. During the next six months she was free of pain, and physical examination revealed no abnormalities on three occasions. Two years later the pain recurred, associated with a slight fever. Still later the patient was referred to us. We found nothing abnormal on abdominal examination but an enlarged uterus. There was a large cystic mass in the right vault. On Nov. 24, 1943, with the patient under nitrous oxide, oxygen and ether anesthesia, an appendectomy, total hysterectomy and bilateral salpingo-oophorectomy were performed. The appendix was short and broad, and the junction of the appendix and cecum was unusually wide, measuring 1.5 cm. Because of its wide base, the appendix was removed between two Kocher clamps and the stump closed with two rows of chromic surgical gut stitches. Both ovaries were destroyed by large endometriomas which were adherent to a uterus containing fibroids and also to the under surfaces of the broad ligaments. The patient made an uneventful recovery.

*The Specimen.*—The distal half of the appendix had intussuscepted into the proximal half, and the invaginated mucosal surface of the tip of the appendix was smooth and glistening and was not ulcerated. The inverted end filled the wide lumen of the appendix, and the tip lay almost at the junction of the appendix and the cecum. In the accompanying drawing the wide base of the appendix is illustrated, as is the relationship between



Showing the wide base of the appendix and the relationship between appendix and cecum. At lower right the slight dimple at the end of the appendix is shown.

the cecum and the appendix. An end on view of the appendix is shown to demonstrate the slight dimple present, and on either side of the dimple there were bluish spots which were undoubtedly small endometriomas. Because of the loss of the appendix before microscopic examination, the diagnosis of endometriosis cannot be substantiated.

The first attack of pain, three years before operation, was undoubtedly acute appendicitis. This inflammatory process may well account for the subsequent development of the intussusception. The recurrence of the pain which necessitated further examination and operation in all probability was due to the intussusception, although the large endometriomas may have played some part in the production of the abdominal pain.

tissue disappeared, and the base of the lesion red clean and granular. On September 30, eight weeks after penicillin therapy was instituted, the lesion completely healed (fig. 1 B).

In this case an acute ulcer with extensive secondary infection responded well to local penicillin therapy. The arterial blood supply to the limb was good and epithelization occurred

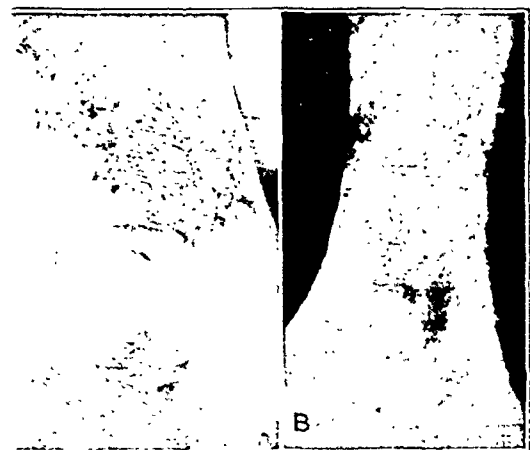


Fig. 1 (case 1).—A, appearance of the ulcer at the beginning of penicillin therapy; B, appearance after treatment for eight weeks.

local applications of gentian violet medication. The ulcer healed after seven months' treatment. She returned to the hospital in February 1941, at which time a high ligation of the saphenous veins and varicose veins were performed. She returned six months later, the ulcer having recurred. The treatment was given, and the ulcer healed in a few weeks. She returned in June 1943 with an ulcer on the right leg and three ulcers on the left leg, which had been present for two months. The granulation tissue in the base of the lesions was covered with a layer of fibrinopurulent exudate (fig. 2 A and C). Hemolytic *Staph. aureus* and *Bacillus proteus* organisms were grown from the surface. There were numerous varicose veins on both legs. A diagnosis of chronic stasis ulcers of the lower extremities was made. Penicillin dressings and Unna's paste boots were applied and changed twice each week. Improvement was rapid, and clean granulation tissue appeared on the base of the ulcers. Within ten days, the small ulcers on the left leg were healed. After seventeen days of treatment, the lesion on the right leg was healed. The larger ulcer on the left leg healed after forty-one days of treatment (fig. 2 B and D).

The lesions in this case had been present for two months. There was extensive infection, but rapid improvement was obtained with penicillin dressings. There was minimal fibrosis around the edges, and as soon as stasis and infection were corrected epithelization occurred rapidly. The previous ulcers had been treated with gen-

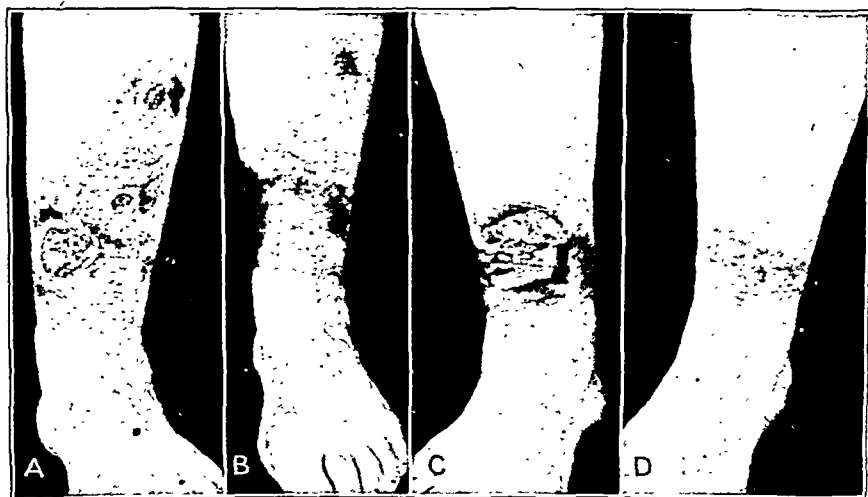


Fig. 2 (case 2).—A, lesions on left leg at the beginning of penicillin therapy; B, lesions on left leg healed after treatment for six weeks; C, lesion on right leg at the beginning of penicillin therapy; D, lesion on right leg healed after treatment for seventeen days.

tion rapidly after the infection and stasis were corrected.

tian violet medicinal, and they healed after periods of seven months and eighteen weeks, respectively. Better results were obtained with penicillin.

CASE 3.—E. McL., a 36 year old Negro woman, had recurrent ulcers on her left leg for three years. She was examined at Duke Hospital in June 1943, and at that time there were two infected ulcers on the medial

CASE 2.—B. M., a 33 year old white woman, had recurrent ulcers of thirteen years' duration on both legs. The first ulcer appeared after pregnancy and persisted for four years. She was examined at Duke Hospital in June 1940, and at that time there was a chronic ulcer which had been present for ten months on her left leg. She was treated with Unna's paste boots and

encroachment on the brain, resulting in severe neurologic symptoms. An unusually good result followed surgical treatment in which laminectomy and suboccipital decompression were done.

*Neurofibromatosis and Osteitis Fibrosa Cystica.*—In an excellent article Thannhauser<sup>5</sup> manifests interest in these conditions. Information continues to be added to the knowledge of them, though in their essential clinical features they are much the same as von Recklinghausen described them. Even he referred to cases with identical features reported by previous authors. The French school, led by P. Marie and H. Bernard, added to the syndrome the pigmentary anomalies of the skin, while the German, English and American literature added the visceral and the osseous changes. Mandl contributed a great advancement in knowledge when he described extirpation of an adenomatous parathyroid gland from a patient suffering from osteitis fibrosa cystica. Knowledge was also added by the physiologic studies of Collip.

Thannhauser clarifies the pathogenesis of osteitis fibrosa cystica localisata and disseminata (von Recklinghausen) and demonstrates that under the heading of osteitis fibrosa cystica Recklinghausen two etiologically different entities are reported: Osteitis fibrosa cystica disseminata is shown to be related by its clinical and histologic features to neurofibromatosis (Recklinghausen); hyperparathyroidism with resulting fibrocystic lesions of bone is primarily caused by hyperfunction or adenoma of one or both parathyroids.

Coburn<sup>6</sup> emphasizes that in cases of parathyroid adenoma the diagnosis is often overlooked and states that this is regrettable because of the brilliant results from early extirpation. He reports a case in detail in which symptoms were manifest over a period of fifteen years.

Ordinarily, after removal of a parathyroid adenoma, the skeleton lesions recalcify. Voltz and Smull<sup>7</sup> report a case, however, in which in five postoperative years this failed to occur, though there was no recurrence of hyperparathyroidism.

5. Thannhauser, S. J.: *Neurofibromatosis (von Recklinghausen) and Osteitis Fibrosa Cystica Localisata et Disseminata (von Recklinghausen)*, *Medicine* 23:105-149 (May) 1944.

6. Coburn, D. E.: *Severe Osteitis Fibrosa Cystica with Parathyroid Tumor*, *Am. J. Surg.* 66:252-258 (Nov.) 1944.

7. Voltz, C. P., and Smull, K.: *Hyperparathyroidism with Failure to Recalcify After Removal of Parathyroid Adenoma (A Case Report)*, *Ann. Int. Med.* 21:329-332 (Aug.) 1944.

Alexander, Pemberton, Kepler and Broders<sup>8</sup> summarize completely most of the knowledge of parathyroid tumors to date. They report 14 cases and lay stress on the widely divergent clinical pictures. It is brought out that the changes in bone appear to be an index more of duration than of severity.

*Osteomalacia.*—Ghormley and Hinchey<sup>9</sup> suggest the use of aluminum acetate in treatment of malacic bone diseases. They present clinical cases of improvement in symptoms and roentgenologic evidence of increase in calcification as justification for its clinical trial and as a stimulus to research. A high percentage of improvement was noted in cases of osteoporosis, osteitis deformans, osteitis fibrosa and osteogenesis imperfecta.

The incidence of renal lithiasis in this series was 60 per cent. In 13, or 92.8 per cent, of the cases, the tumor showed cytologic evidence of malignancy. The malignant nature of the tumors makes complete removal imperative, according to the authors. It is therefore not advisable to leave tissue to avoid tetany, as this condition can be controlled with calcium and vitamin D.

*Fibrous Dysplasia of Bones (Albright Syndrome).*—Dockerty, Meyerding and Wallace<sup>10</sup> report the thirty-fourth case in the literature since the description of fibrous dysplasia of bones in 1937 by Albright. In the case presented there was the characteristic triad of rather dissociated manifestations, consisting in disseminated fibrosis of bone, patchy cutaneous pigmentation and precocious puberty in females.

*Osteogenesis Imperfecta.*—For some time, discussion has centered around the question as to whether osteogenesis imperfecta (Vrolik), in which there are intrauterine fractures, differs from the Lobstein type, in which only postnatal fractures occur. Rosenbaum<sup>11</sup> reports cases of the two types in the same family, tending to disprove the duality of the syndromes as propounded by Glanzmann. In addition, he found

8. Alexander, H. B.; Pemberton, J. deJ.; Kepler, E. J., and Broders, A. C.: *Functional Parathyroid Tumors and Hyperparathyroidism*, *Am. J. Surg.* 65:157-188 (Aug.) 1944.

9. Ghormley, R. K., and Hinchey, J. J.: *The Use of Aluminum Acetate in the Treatment of Malacic Diseases of Bone*, *J. Bone & Joint Surg.* 26:811-817 (Oct.) 1944.

10. Dockerty, M. D.; Meyerding, H. W., and Wallace, G. T.: *Albright Syndrome (Fibrous Dysplasia of Bones, with Cutaneous Pigmentation in Both Sexes and Gonadal Dysfunction in Females)*, *Proc. Staff Meet., Mayo Clin.* 19:81-88 (Feb. 23) 1944.

11. Rosenbaum, S.: *Osteogenesis Imperfecta and Osteopsathyrosis*, *J. Pediat.* 25:161-167 (Aug.) 1944.

oped in this region and failed to heal. Within months after injury, two other ulcers developed. Fungus infection was suspected, and the patient was given numerous roentgen ray treatments over the lower leg. This resulted in pronounced induration and fibrosis of the skin over the entire leg. Numerous ointments were used locally, and elastic stockings were worn to prevent stasis, but the ulcers failed to heal. He was seen at Duke Hospital on July 26, 1944, and examination revealed four ulcerations varying from 0.5 to 5 cm in diameter over the anterior surface of the left leg. They were surrounded by extensive fibrosis, and the ulceration tissue was covered with fibrinopurulent exudate (fig. 10 A). Hemolytic *Staph. aureus* organisms were grown from the surface of the ulcers. A Wassermann test elicited a negative reaction. Pathologic section of a biopsy specimen taken from the edge of the largest ulcer revealed chronic nonspecific inflammation. No fungus organisms were seen. A diagnosis of chronic stasis ulcers was made. The patient refused operation. Penicillin dressing and an Unna paste boot were applied and changed weekly. There was rapid improvement. The small ulcer at the lower end of the leg healed in one week, the lesion on the upper part of the leg healing in three weeks. The two ulcers in the center healed much more slowly. The small lesion healed in four months, and the larger one had not completely healed after eight months' treatment. Another small ulcer subsequently appeared after eczematoid dermatitis. Figure 10 B shows the condition of the large ulcer after a period of eight months' treatment. Little infection is present, but the granulation tissue was scanty because of poor arterial blood supply.

This case is similar to the one previously presented. The infection cleared rapidly after penicillin was applied, and it is thought that slow healing was due to poor arterial blood supply. Palliative treatment in such cases is not satisfactory.

#### COMMENT

The management of chronic stasis ulcers of the lower extremities is difficult. Palliative treatment is justified in some cases, and the methods used for the ambulatory patient consist of elastic support of the extremity to relieve the enormous hydrostatic pressure and topical applica-

tion of a bacteriostatic agent to combat infection. In 10 cases penicillin was used topically as a bacteriostatic agent. Elastic support was supplied to the extremity by application of Unna's paste boots. The local infection in all cases subsided rapidly after the application of penicillin. Penicillin appeared to be far superior to other bacteriostatic agents in cases in which there had been previous treatment. The infection was controlled more readily when the dressings were changed twice each week. This was probably due to the fact that penicillin loses its strength after being at body temperature for several hours. Rapid healing occurred in 5 cases of early ulceration in which there was minimal fibrosis around the edges and good arterial blood supply. The time required for healing in these cases varied from ten days to ten weeks. In 1 case the patient failed to return for treatment until the lesion was healed, but when she was last seen the infection was under control and epithelization was occurring rapidly. Healing in the other 4 cases was slow, although the infection was under control. This was thought to be due to poor arterial blood supply. It is my opinion that in such cases treatment should be radical excision of the ulcer and covering of the defect with a skin graft, unless operation is contraindicated.

#### CONCLUSIONS

The secondary infection in chronic stasis ulcers responds readily to topical applications of penicillin. It is thought to be superior to other bacteriostatic agents that are generally used for this purpose. In the early stages rapid healing occurs when the infection and stasis are controlled. Healing is delayed in the cases of chronic ulceration because of extensive fibrosis of the edges and poor arterial blood supply.

Holm<sup>19</sup> calls attention to the lines formed in growing bones as a result of phosphorus poisoning and shows by roentgenograms that they may last a lifetime.

*Ligaments, Muscles and Tendons.*—Kuhns<sup>20</sup> points out that ligamentous weakness is present and easily discernible as a clinical entity in 10 per cent of children but that ligamentous tightness is also present in many and has received scant attention. Tightness is found more frequently in the hamstring and back areas.

Goldberg and Comstock<sup>21</sup> emphasize the differential diagnosis of herniations of muscle observed in the legs from lipoma, hematoma, tuberculosis, pseudo hernia and varices. A case of multiple small hernias of the tibialis anterior muscles of both legs is presented.

In an analysis of 190 cases of chronic non-specific tenosynovitis and peritendinitis, Lipscomb<sup>22</sup> feels that trauma is in most instances the etiologic factor. The pathologic changes are reviewed, and his opinion is that they differ only in degree and depend on the duration of the disease primarily. Conservative treatment consisting in splinting and roentgen ray therapy is advised, and if improvement does not occur surgical intervention is indicated.

19. Holm, O. F.: Beitrag zur Kenntnis der Entstehung der Phosphorsklerose, Acta radiol. 23:549-561, 1942.

20. Kuhns, J. G.: Tightness of Ligamentous Structures, Arch. Pediat. 61:179-183 (April) 1944.

21. Goldberg, H. C., and Comstock, G. W.: Herniation of Muscles of the Legs, War Med. 5:365-367 (June) 1944.

22. Lipscomb, P. R.: Chronic Nonspecific Tenosynovitis and Peritendinitis, S. Clin. North America 24: 780-797 (Aug.) 1944.

*Osteochondritis.*—Uhry<sup>23</sup> presents an interesting review of 79 cases of osteochondrosis of the tuberosity of the tibia (Osgood-Schlatter's disease) and defends the original ideas of the persons first describing the condition in which the disorder develops as a result of minor separation of the structures of the tibial tubercle and the patellar ligament. The author believes that the characteristic pathologic changes represent callus repair at the site of separation. He feels that osteochondritis as such (that is, inflammation) is not in evidence. The immediate instigating factor is consistently trauma.

*Sudeck's Atrophy.*—Buchman<sup>24</sup> reports an interesting case of Sudeck's atrophy following a single minor surgical procedure for exploration of a tendon sheath. The surgical treatment was followed by severe symptoms, partially relieved by injection of procaine hydrochloride after lack of response to usual methods of treatment.

*Abuse of Bed Rest.*—Since this article will probably not come within the purview of the editors of other sections of "Progress in Orthopedic Surgery," it is felt that it should be mentioned here. Ghormley<sup>25</sup> sounds a keynote of change from the emphasis placed on rest by Hugh Owen Thomas and cites the many disadvantages of rest as compared with early activity in the orthopedic field.

23. Uhry, E., Jr.: Osgood-Schlatter Disease, Arch. Surg. 48:406-414 (May) 1944.

24. Buchman, J.: Postoperative Post-Traumatic Osteoporosis or Sudeck's Atrophy, Bull. Hosp. Joint Dis. 4:55-61 (Oct.) 1943.

25. Ghormley, R. K.: Abuse of Rest in Bed in Orthopedic Surgery, J. A. M. A. 125:1085-1087 (Aug. 19) 1944.

## II. CONGENITAL DEFORMITIES

PREPARED BY J. HIRAM KITE, M.D., ATLANTA, GA.

For several years I have begun this section on "congenital deformities" with a description of the experiments conducted by Josef Warkany. Each year he and his workers have given additional information on the cause of some of the congenital deformities. This past year has brought information on how to prevent deformities.

In times past, various authors have attributed congenital malformations to a maternal nutritional deficiency. Warkany and Schraffenberger,<sup>26</sup> after establishing a set pattern of deformities which follow what they call diet I, made

various additions to the diet, trying to prevent deformities. They found first that 2 per cent pig liver would prevent deformities. A search was made for the preventive factor in pig liver. After studying hundreds of litters of rats, they give the following conclusions:

The congenital malformations of the pattern of diet I are prevented when the maternal diet I is supplemented by riboflavin. Supplements of thiamine hydrochloride, nicotinic acid, pyridoxine and calcium pantothenate are not preventive. With a purified maternal diet in which the vitamin B complex is represented by crystalline substances, malformations of the pattern of diet I appear in the offspring when riboflavin is omitted. On the same diet supplemented by

26. Warkany, J., and Schraffenberger, E.: Congenital Malformations Induced in Rats by Maternal Nutritional Deficiency, J. Nutrition 27:477 (June) 1944.

*Operation.*—A thoracotomy on the left side with the patient under endotracheally induced oxygen and ether anesthesia was made, and the chest was opened through the ninth interspace. There was no damage to the lung or diaphragm, but the base of the lung was firmly adherent to the diaphragm.

A large incision was made into the abdominal cavity through the diaphragm. A large amount of blood and clot was found within the abdominal cavity. The spleen, which was about three times its normal size, was bleeding profusely from a complete tear through the lower pole and several fractures near the hilus. The spleen was extremely friable and was attached in many places. It was freed from the surrounding structures, and the pedicle was clamped, divided and ligated with no. 2 chromic surgical gut. The stomach and colon were found to be normal. The diaphragm was closed in layers with 0 chromic surgical gut. The chest wall was closed in layers with 0 chromic surgical gut. One drain was placed into the chest at the posterior costophrenic angle and sealed under water. The immediate postoperative condition was good.

*Pathologic Report.*—Description of Tissue: The specimen consisted of a spleen measuring 20 by 16 by 5 cm. and weighing 600 Gm. The hilar surface showed a stellate tear with transcapsular rupture of the spleen. A small piece of spleen, measuring 4 by 5 by 2.5 cm., arrived separate—apparently it had been torn from the main substance of the spleen.

*Microscopic Observations:* Sections were composed of splenic tissue showing evidences of hemorrhage, particularly beneath the capsule in one area. The malpighian follicles appeared to be increased in number and size. An increase of the reticuloendothelial cells was present both in the follicles and in the sinuses. A large number of reddish brown pigmented cells were

present. Impression smears of the fresh splenic tissue stained with Wright's stain revealed the presence of *P. vivax*.

*Chief Diagnosis.*—The injury was diagnosed as transcapsular rupture of a malarial spleen.

*Subsequent Course.*—A duodenal tube was used for twenty-four hours and 1,000 cc. of blood was given to the patient on the first postoperative day. He was given a full diet on the third postoperative day. The intercostal catheter was removed on the fifth day, and the patient was out of bed on the eighth day. Active antimalarial therapy was carried out during convalescence, and a blood smear was negative for parasites when the patient was transferred to an Italian hospital, on the tenth day, for further convalescence.

#### COMMENT

This was our first experience with the trans-thoracic route for an injury known to involve exclusively an intra-abdominal organ. This approach was chosen deliberately, and we feel the choice to be justified both by the ease of removal and by the smooth and rapid convalescence. It was the operator's opinion that the use of an abdominal incision would have made splenectomy more difficult. Before the war we witnessed the removal of malarial spleens by the abdominal route and were impressed by the difficulties encountered. It is also of interest that the diagnosis of malarial involvement of the spleen was made preoperatively.

att, Zeldes and Goodfriend.<sup>30</sup> They pointed out that in 1927 Fairbank described "stippled epiphyses" associated with dwarfism, but he failed to recognize thyroid deficiency as the basis of the disturbance. Ten years later Reilly and Smythe described 5 similar cases, designating the condition as "cretinoid epiphysial dysgenesis." McCullough and Sutherland in 1940 described stippled epiphyses in a dwarf in whom there was no sign of hypothyroidism and used the term "epiphysial dysplasia punctularis" to designate the skeletal change. Wilkins, who found bilateral epiphysial dysgenesis in 23 of 25 children with hypothyroidism, said that he had never seen true dysgenesis in any type of dwarfism other than that occurring with hypothyroidism.

In roentgenograms epiphysial dysgenesis is diagnosed by the appearance of multiple small irregular islets of calcification, scattered over a considerable area. The islets are irregularly spaced, and the anatomic distribution does not conform to that of the normal centers of ossification. As the islets grow larger or as new ones occur, they appear to coalesce and give the impression of a single large center which has undergone fragmentation. The defect is apparently due to an abnormality of endochondral ossification.

Roentgenologically, epiphysial dysgenesis may be confused with osteochondritis deformans. However, the latter usually occurs in epiphyses which previously have appeared normal on roentgen examination. Furthermore, osteochondritis deformans (Legg-Calve Perthe's disease, Osgood-Schlatter disease) is usually unilateral, occurring most frequently in only one epiphysis. It is generally accompanied with pain and does not respond to thyroid therapy.

[Ed. Note (L. D. B.).—Osteochondritis or osteochondrosis is frequently bilateral.]

Achondroplasia fetalis may be confused with cretinism clinically, but the latter may be differentiated by the unique deformities of the metaphyses and shafts of the long bones and the grossly abnormal shapes of the epiphyses.

Carl Badgley<sup>31</sup> advances the theory that the pathogenesis of the multiple deformities occurring in arthrogryposis multiplex congenita may best be explained on the basis of arrest of embryonic development. A primary pathologic change of the muscle, which has been proved

inherent in lambs but which is of unknown origin in human beings, can well be the causative factor of this arrest. The normal rotation of the limb buds, an intrinsic characteristic of the human fetus, is carried out by the muscles of the extremity. The loss of muscle function arrests or prevents this rotation. The resultant club foot, club hands and postural deformities are the retained posture normal for the 3 month fetus but arrested from rotation into the characteristic human attitude. The rigidity of the joints is similarly the result of failure of muscle function, preventing normal fetal motion in otherwise normally developing joints.

Correction of the deformities by release operations to reestablish mobility and to continue rotation of the extremities to the normal posture of mature human extremities is the aim of therapy. The muscular damage is of course irreparable, but pronounced improvement in function can be obtained. Early treatment, with early operative correction of the deformities if necessary, is advised.

[Ed. Note (L. D. B.).—Attempts at correcting arthrogryposis deformities are sometimes most discouraging.]

Lyons and Sawyer<sup>32</sup> report a case of cleidocranial dysostosis in a veteran of World War I. They say that cleidocranial dysostosis is a comparatively rare congenital defect of the bony skeleton. Less than 100 cases have been reported in the literature. It is a syndrome in which the chief characteristic observation is a complete or partial absence of one or both clavicles. As so often happens, when one congenital defect is found in the body, another may also be found. In this condition one of the more constant defects accompanying that of the clavicles is a variation in the development of the bones of the skull. Barlow in 1883 reported a case of congenital absence of the clavicles and malformation of the cranium in a girl aged 2 years, probably the first typical case described. In 1897 Marie and Sainton reported 4 cases and applied the term "hereditary cleidocranial dysostosis" to the anomaly syndrome. Fitchet in 1929 made a complete survey of all reported cases in the literature. He stated that the chief features of this syndrome are grouped under four headings as follows: aplasia, more or less pronounced, of the clavicles; exaggerated development of the transverse diameter of the cranium; delay in the ossification of the fontanels, and hereditary transmission. Fitchet expressed the belief that the term "hereditary cleidocranial dysostosis" should be discontinued and "congenital cleidocranial dysostosis" should be used.

30. Blatt, M. L.; Zeldes, M., and Goodfriend, J.: Epiphysial Dysgenesis Associated with Cretinism in a Premature Infant, *Am. J. Dis. Child.* 67:480 (June) 1944.

31. Badgley, C. E.: Rehabilitation in Cases of Arthrogryposis Multiplex Congenita, *Arch. Phys. Therapy* 24:733 (Dec.) 1943.

32. Lyons, C. G., and Sawyer, J. G.: Cleidocranial Dysostosis, *Am. J. Roentgenol.* 51:215 (Feb.) 1944.



**Blood Volume Studies:** Studies of blood volume were made only for dog 239. The results are shown in table 8 and discussed in connection with those of group 2.

TABLE 3.—*Changes in Red Cell Volume and Oxygen Content (in per Cent of the Control Values) of Whole Blood from Representative Dogs of Group 1*

Experiment No.	Sample No.	Time After Section, Hr.	Cell Volume, %	O <sub>2</sub> Content, mM/Liter of Blood	Cell Volume, Δ %	O <sub>2</sub> Content, Δ %
239 (Series A)	Control	0	52.5	9.18		
	2	1	.....	.....	-21.2	-20.4
	3	3	.....	.....	-28.2	-22.7
	4	6	.....	.....	-29.9	-23.1
	5	12	.....	.....	-33.3	-16.1
	6	22.5	.....	.....	-25.7	-24.4
	7	28.5	.....	.....	-26.3	-23.7
230 (Series B)	Control	0	47.8	8.91		
	2	1	.....	.....	-11.9	+ 2.7
	3	3	.....	.....	-15.9	-11.7
	4	6	.....	.....	-14.8	- 9.8
	5	12	.....	.....	- 9.2	.....
	6	23	.....	.....	- 7.7	+10.3

control values with those following the cutting of the cord, the results have been expressed in per cent change of the original concentration ( $\Delta H_2O$ ,  $\Delta Cl$ , etc.). The concentration of water and electrolytes in the red cells was calculated from the analysis of whole blood. When the values obtained after cutting of the cord are compared with the control values, the most significant differences found are the lowered serum protein and carbon dioxide content and the decreases in the cell volume and oxygen content.

In table 5 the analyses of skeletal muscle, liver and skin from dog 239 are given. It is noteworthy that the total water content of the tissues analyzed did not decrease but remained within limits of normal values. In the muscle, there was a decrease in the extracellular fluids associated with a swelling of the muscle cells. This is an instance of dehydration in the sense that the extracellular phase has been diminished. The

TABLE 4.—*Changes in Water, Electrolytes and Protein Concentrations (in per Cent of the Control Values) in the Serum and Erythrocytes of Two Representative Dogs from Series A and B of Group 1 Following Experimental Section of the Spinal Cord*

Values are expressed in units per liter.

Experiment No.	Sample No.	Time After Section, Hr.	Serum or Cells	pH	Total CO <sub>2</sub> , mM	H <sub>2</sub> O, Gm.	Cl, mM	Na, mM	K, mM	Ca, mM	Mg, mM	Total Protein, Gm.
239, Series A	Control	0	Serum	7.38	15.67	932.6	114.1	141.5	3.67	2.65	1.03	61.1
				±	Δ %	Δ %	Δ %	Δ %	Δ %	Δ %	Δ %	Δ %
	2	1	.....	—	+14.12	+0.41	+1.23	+0.21	-7.36	+6.79	-8.74	-11.61
	3	3	.....	—	+20.83	+1.19	-0.09	-1.90	-7.36	+11.33	-3.89	-9.66
	4	6	.....	—	+26.20	+1.17	-2.28	-4.44	-15.89	+5.66	+2.91	-9.17
	5	12	.....	—	+17.88	+0.83	-2.72	-4.72	-14.45	+9.44	+11.65	-11.61
	6	22.5	.....	+0.05	+ 8.17	+0.59	-2.72	-3.46	-13.07	+13.96	+21.39	-13.25
	7	28.5	.....	-0.01	- 5.05	+0.27	-2.28	-4.72	-3.0	+22.65	+23.30	-16.35
	Control	0	Erythrocytes	.....	.....	Gm. 729.0	mM 69.4	mM 103.3	mM 9.03			
						Δ %	Δ %	Δ %	Δ %			
	2	1	.....	.....	.....	-2.33	-35.4	-18.3	-12.5			
	3	3	.....	.....	.....	-3.71	-12.8	- 3.2	-15.8			
	4	6	.....	.....	.....	-2.61	-17.0	- 9.8	+20.5			
	5	12	.....	.....	.....	-0.96	-17.0	- 4.8	+11.3			
	6	22.5	.....	.....	.....	-1.65	-11.5	-20.3	-11.0			
	7	28.5	.....	.....	.....	-0.96	-18.0	-22.2	-10.2			
230, Series B	Control	0	Serum	7.40	—	935.7	110.7	147.7	3.82	2.66	0.90	63.2
	2	1	.....	.....	21.33	.....						
				Δ ±	Δ %	Δ %	Δ %	Δ %	Δ %	Δ %	Δ %	Δ %
	2	1	.....	-0.06	—	+1.10	+3.16	-2.98	+4.19	—	—	-11.55
	3	3	.....	+0.02	+10.02	+1.20	+2.53	-3.66	-11.60	—	—	-15.20
	4	6	.....	—	—	+0.95	+2.26	-4.34	+19.37	—	—	-17.55
	5	12	.....	—	—	+0.97	+0.45	-3.16	+42.4	—	—	-10.29
	6	23	.....	+0.02	—	+0.50	+1.36	-4.81	+59.7	—	—	- 6.65
	Control	0	Erythrocytes	.....	.....	Gm. 710.2	mM 65.7	mM 101.7	mM 10.47			
						Δ %	Δ %	Δ %	Δ %			
	2	1	.....	.....	.....	-0.80	-1.50	-19.38	+1.60			
	3	3	.....	.....	.....	+1.00	-8.40	-1.48	+3.10			
	4	6	.....	.....	.....	-2.82	+0.15	+13.09	+8.00			
	5	12	.....	.....	.....	-0.31	-3.45	-0.54	+4.33			
	6	23	.....	.....	.....	-5.44	-16.20	-15.95	+10.05			

**Electrolyte, Water and Protein Content of Serum, Erythrocytes and Tissues:** In tables 3, 4 and 5 are presented the values in detail of electrolyte, water and protein content of serum, erythrocytes and tissues for 2 representative dogs of this group. To facilitate comparison of the

circulatory space, as determined by hemoglobin methods in the muscle, was 92 cc. per kilogram, which is more than the mean average value of 71 cc. for muscle from normal dogs. This may indicate either a trapping of erythrocytes in the tissue or else a sluggish flowing of blood into

bell and Grice,<sup>37</sup> from Boston, describe the modification of the Denis Browne splint for the treatment of congenital club feet. They use a splint which is narrower in the heel and makes the foot better and is also arched to prevent the rocker bottom. They have made an improvement in the method of strapping the foot to the splint. They give the following summary:

During the treatment of 53 patients with complicated congenital talipes equinovarus with the modified Denis Browne splint, several refinements in technic have been evolved to meet various problems, such as pressure sores, dermalis, incomplete correction, persistent equinus deformity, loss of longitudinal arch and unilateral deformity. These refinements are described. Success of this method depends on the accuracy with which the foot is fixed to the splint. If properly applied, the splints will allow correction

of the varus deformity and yet will maintain the longitudinal arch while obtaining full correction of the equinus deformity. Recurrence of the deformity is a constant threat, but this tendency is minimized by complete correction early and then by continued use of the splint intermittently, at least until the child begins to walk.

[ED. NOTE (J. H. K.).—For the last two years I have commented at length on my experiences with the Denis Browne splint. Briefly, I have obtained better results with plaster. I have tried the method of strapping mentioned by the author and feel that it is an improvement. Denis Browne says that he has made more than fifty modifications of the splint. Still more may be expected.]

[ED. NOTE (L. D. B.).—I have seen Grice apply the modified splint and have seen several of the patients. The splint and the method of applying the adhesive are great improvements in the Denis Browne technic, and any one using splint therapy should adopt these modifications.]

37. Bell, J. F., and Grice, D. S.: Treatment of Congenital Talipes Equinovarus with the Modified Denis Browne Splint, *J. Bone & Joint Surg.* 26:799 (Oct.) 1944.

### III. TUMORS OF BONE AND OF SYNOVIAL MEMBRANE

PREPARED BY HENRY W. MEYERDING, M.D., ROCHESTER, MINN.

A. *Classification of Tumors of Bone.*—Brachetto-Brian<sup>38</sup> presents a classification adopted by the "Comité para el Estudio de los Tumores Oseos" of the Asociación Argentina de Cirugía.

He discusses various phases and believes that the classification should be based on the type of tissue affected, since different cells would originate different neoplasms. The classification is as follows:

	Genetic Cells	Neoplasms Originated		Names of Tumors
A. Tumors of the skeletal sector	Osteoblast	I. Osteoblastoma	Benign Malignant	Osteoma Osteosarcoma; osteogenic sarcoma
	Chondroblast	II. Chondroblastoma	Benign Malignant	Chondroma Chondrosarcoma
	Myeloplax	III. Myeloplaxoma	Benign Malignant	Giant cell tumor
B. Tumors of the reticulo-endothelial sector	Mesoblast Histocyte Reticuloblast	IV. Reticuloblastoma	Benign Malignant	Reticulosarcoma Ewing's sarcoma
C. Tumors of the hematopoietic sector	Angioblast Mesoblast Hemohistioblast	V. Myeloblastoma		Kahler's disease; myeloma
D. Tumors of the vascular-connective sector	Hemocyto blast	VI. Fibroma and so forth	Benign	
	Mesoblast	VII. Osteosarcoma	Malignant	
	Fibroblast Angioblast			

In the following tabulation these seven groups of neoplasms are represented with their varieties:

A. Tumors of the skeletal sector	I. Osteoblastoma	Benign	1. Benign osteoblastoma of the substantia spongiosa 2. Benign sclerosing osteoblastoma 3. Benign chondro-osteoblastoma
		Malignant	1. Malignant osteogenic osteoblastoma 2. Malignant osteogenic osteoblastoma with myeloplaxes 3. Secondary malignant osteogenic osteoblastoma 4. Juxtaconjugal malignant osteogenic osteoblastoma 5. Telangiectatic malignant osteogenic osteoblastoma
	II. Chondroblastoma	Benign	1. Chondroblastoma 2. Chondromyxoblastoma
B. Tumors of the reticulo-endothelial sector	III. Myeloplaxoma	Malignant	1. Malignant chondroblastoma 2. Benign myeloplaxoma
		.....	2. Malignant myeloplaxoma
	IV. Reticuloblastoma	Benign	1. Localized reticuloendothelioma
		Malignant	1. Undifferentiated reticulosarcoma 2. Differentiated reticulosarcoma

38. Brachetto-Brian, D.: La clasificación adoptada en el "comité para el estudio de los tumores oseos." *Rev. Prensa méd. argent.* 28:2185-2190 (Nov. 19) 1941;

abstracted, *Arch. cubanos cancerol.* 3:19-26 (Jan.-March) 1944.

In dog 239, group 1, at the end of six and one-half hours, the extreme reduction of red cell mass was accompanied with a less noticeable reduction in plasma volume.

**Electrolyte, Water and Protein Content of Serum and Erythrocytes:** In tables 9 and 10 are presented the analytic and calculated data in detail relating to the electrolyte, water and protein content of the serum and the erythrocytes for 3 representative experiments from the second group of animals. Since the values for the two groups are similar, they are considered here together. In group 2, as in group 1, the significant changes found in the blood were the lowered serum protein content and the decreases in the cell volume and oxygen content. These alterations indicate hemodilution, which might have been a result of the entrance of extracellular or intracellular water from elsewhere in the body. They were not the result of extensive loss of blood during section of the cord. The plasma volume was not increased for a number of hours following the operation, which suggests that interstitial fluid had not entered the circulating system. This deviation may be a result of either the trapping of red cells or the collapsing of blood vessels because of the prevailing low blood pressure, large numbers of red cells being retained thereby, as evidenced by a greatly decreased cell volume. Such action would be expected to decrease the original blood volume. This was verified experimentally. If interstitial fluid had entered the now decreased vascular system, the tissues of the body should have become dehydrated. On the contrary, skeletal muscle, liver and skin did not change in total water content. Even if some interstitial fluid did enter the vascular system, it was not enough to account for the lessened proteins; therefore, the most likely way to account for this change was that some protein must have been lost through the vascular membranes. It is to be noted that the serum water values never decreased very much. In a number of animals the serum water increased from 1 to 2 per cent and was accompanied with a loss of water from the red cells, which were attempting to restore osmotic equilibrium.

In all experiments the changes in serum sodium and chloride concentrations were small. This observation holds for the red cells, too, except for dog 239, in group 1, in which the cell chloride and sodium concentrations decreased sharply. The decrease in chloride could result in part from the low carbon dioxide tension existing in the serum of this animal. The chloride was not decreased from excretion in the urine, since oliguria was present.

The data for serum potassium from all animals in group 2 and series B of group 1 showed a decided rise. The dogs of series A, group 1, showed a decrease in the values for potassium. The highest concentration of serum potassium was found in the animals in which blood had leaked into the lumen of the intestine. In no instance was the potassium of such a concentration as to have toxic effects on the heart, although it might have been a contributing factor in retarding the recovery of the animals in group 2.

The values for calcium of the serum of all dogs, except dog 239, were lower after the cutting of the cord, compensating for the change in the protein level, as total calcium must vary with total protein if calcium ion concentrations are to be held within physiologic limits.

#### COMMENT

The general effects of section of the spinal cord at the eighth cervical segment for the first six to twelve hours were the same in both groups of experiments. In group 1 the further decline of blood pressure and the failure of the circulation subsequent to this period are to be explained principally by the withholding of fluids and food and the maintenance of the animals in the dorsal position on the table.<sup>6</sup> The presence of the two small wounds in the legs did not appear to be an important factor, even though there was some infection present. The remarkable feature about the circulation during this period was the persistence of the blood pressure at extremely low levels for long periods before circulatory failure and death came about.

In group 2, in which fluids and food were given postoperatively, the significant feature was the persistence of the blood pressure in the vicinity of critical levels during the initial period of spinal shock and for four to six days thereafter, without the development of surgical shock and with subsequent gradual recovery.

The strong resistance of the animals of both groups to the low blood pressures under conditions of the two types of experiments is best explained by the fact that with the arterioles and capillaries dilated and with but little loss of blood from operation, the tissues received a larger supply of blood and were better nourished than the level of blood pressure alone would indicate; consequently, surgical shock and death came relatively late in group 1 and were avoided in

6. Eversole, J. W.; Kleinberg, W.; Overman, R. R.; Remington, J. W., and Swingle, W. W.: *Am. J. Physiol.* 140:490, 1944.

symptoms, as well as partial recalcification of some of the defects of bone.

Henschen<sup>47</sup> reports a case of eosinophilic granuloma, in which excision of the lesion from the left mandible of a man 24 years of age was done, followed by recurrence and second operation. He feels that every destructive lesion of bone in adolescents should be suspected of being eosinophilic granuloma.

Cavalcanti<sup>48</sup> reviews the literature on post-traumatic epidermoid cysts and presents a case in which there was involvement of a phalanx of the right middle finger. The lesion was excised and found to be a typical epidermoid cyst on examination.

Pohlmann and Wachstein<sup>49</sup> mention that epidermoid (squamous epithelial) bone cyst of the phalanges, a rare tumor of bone, has been reported as proved in only 10 cases. They present a review of the 10 cases in the literature and an additional case of their own and advocate removal of the cyst and cauterization of the cavity, measures which preserve the finger and prevent possible recurrence of the lesion.

*C. Lesions of Synovial Membrane.*—Moretz<sup>50</sup> reports 4 cases of malignant tumors arising from synovial membrane. He mentions that this type of lesion is classified according to the microscopic picture. Some lesions apparently arise from the outer layers of the synovial tissue and are indistinguishable from fibrosarcoma, and the others arise from the inner layers, thus presenting a more epithelioid type. Both types of tumor cells may be present in the same lesion. The prognosis in any case is unfavorable. Amputation is recommended except in those cases in which conditions are favorable for a wide local excision of the lesion or in those in which there is local recurrence.

*D. Benign Neoplasms of Bone.*—Osteoid osteoma: Stauffer<sup>51</sup> presents a case of osteoid osteoma, in which the lesion was excised from the head of the radius, with complete relief of symptoms. The previous pathologic report had been "healing benign giant cell tumor."

Harmon<sup>52</sup> presents a case of osteoid osteoma. The patient was a girl 9 years of age, and the lesion was located in the midportion of the femoral shaft. All laboratory tests gave normal results. At operation a soft gritty material was found in the cavity. Cultures revealed no growth. The microscopic examination revealed osteoid tissue between hypertrophic trabeculae with fibrous reaction and no inflammatory cells.

Kleinberg<sup>53</sup> reports 3 cases of osteoid osteoma, one lesion being located in the upper end of the fibula, one involving the lamina of the second lumbar vertebra and one in the neck of the astragalus. He states that the patients had complete relief of all symptoms following excision of the lesion.

Lewis<sup>54</sup> presents 11 cases of osteoid osteoma, in 9 of which the condition was proved and in 2 probably proved. The lesions conformed to the clinical and roentgenologic criteria of Jaffe and Lichtenstein. He advocates simple block removal of the nidus or focus of infection and feels that failure to remove all of this may cause persistence of the symptoms.

[ED. NOTE.—Such case reports as the foregoing are of increasing value and interest to physicians. Jaffe and Lichtenstein have incited a great deal of interest among surgeons, especially orthopedic surgeons, through their studies of this condition. An increasing number of case reports are evident in the literature. In the past the lesion was considered a focus of infection described as nonsuppurative osteomyelitis of Garré, Brodie's abscess or localized subcortical abscess of bone. There still exists among surgeons and pathologists a difference of opinion regarding the lesion.]

Periosteal Fibroma: Sgrosso<sup>55</sup> presents a case in which the patient was an 11 year old boy and the huge lesion involved the humerus. Operation had been performed unsuccessfully three months prior to the patient's admission to the hospital. The huge fibroma was removed with good results, a rare condition.

Periosteal Lipoma: Cottini<sup>56</sup> presents a case of periosteal lipoma of the radius, the patient being

47. Henschen, C.: Das eosinophile Granulom des Knochens, Schweiz. med. Wchnschr. 73:451-455 (April 10) 1943.

48. Cavalcanti, J.: Cisto epidermoide post-traumático de dêdo, Arq. brasil. de cir. e ortop. 11:36-41, 1943.

49. Pohlmann, H. F., and Wachstein, M.: Epidermoid (Squamous Epithelial) Bone Cyst of Phalanx, Ann. Surg. 119:148-154 (Jan.) 1944.

50. Moretz, W. H.: Malignant Tumors Arising from the Synovial Membrane with Report of Four Cases, Surg., Gynec. & Obst. 79:125-132 (Aug.) 1944.

51. Stauffer, H. M.: Osteoid-Osteoma of the Head of the Radius: Case Report, Am. J. Roentgenol. 52:200-202 (Aug.) 1944.

52. Harmon, P. H.: Osteoid Osteoma of Mid-Shaft Region of Femur, Am. J. Surg. 66:128-131 (Oct.) 1944.

53. Kleinberg, S.: Osteoid Osteoma, Am. J. Surg. 66:396-401 (Dec.) 1944.

54. Lewis, R. W.: Osteoid-Osteoma: A Review of Portions of the Literature and Presentation of Cases, Am. J. Roentgenol. 52:70-79 (July) 1944.

55. Sgrosso, J. A.: Fibroma perióstico del húmero, Rev. ortop. y traumatol. 13:198-204 (April) 1944.

56. Cottini, C. F.: Consideraciones sobre un caso de lipoma perióstico de radio, Bol. y trab., Soc. argent. de cirujanos 4:700-707, 1943; abstracted, Rev. Asoc. méd. argent. 57:995-997 (Nov. 30) 1943.

weeks the spinal wounds were healed and the pulse, respirations and temperatures had returned to normal ranges. The postoperative course was uneventful up to the time of termination of the experiments, except for a mild cystitis in dog 238, which was healing at the time of death. Occasional small pressure sores appeared on the hips, but they healed rapidly under proper care and never became an influential factor on the general condition of these animals.

Incontinence of stools was established soon after operation, and by the fourth to the sixth day the bladder had started to empty involuntarily. There was no gross evidence of blood in the stools of any of the animals. Flexor and knee jerk reflexes had been regained almost immediately after section of the cord in all experiments, but flaccid paralysis of the hindquarters was complete. In dog 234 slight extensor tone became manifest toward the latter part of the second month, and by the time of killing, one hundred and nineteen days after section, it had become sufficiently strong to support momentarily the weight of the animal when placed on its feet. Throughout the course of the experiments, the body weights, with but 1 exception, remained constant or showed a slight increase (table 1).

TABLE 1.—Body Weights in Kilograms of Five Dogs Taken at Varying Intervals Following Experimental Section of the Spinal Cord at the Eighth Cervical Segment

Days After Section	Dog 234	Dog 234	Dog 302	Dog 237	Dog 238
0	8.9	13.0	15.0	14.0	11.4
7	8.9	12.1			
10-15	9.0	12.8	15.8		11.6
22-24	9.2	12.8	16.4	12.7	
33-39	8.9	13.9	16.3	11.8	
41-43	8.8	14.2	16.1		
50-64	8.4	14.1	17.3		
69-72	8.9	14.3	16.9		
74-77	...	14.7	17.0		
87	8.9				
119	8.8				
	Killed 119th day	Killed 74th day	Killed 77th day	Killed 89th day	Killed 13th day

Disuse atrophy in the hindquarters became apparent after the first month, however, and by the time that dog 234 was killed the muscles were greatly wasted, and necropsy revealed the cortex of the femurs to be extremely thinned. Function of the forelegs was not intensely disturbed in any of the animals and became sufficiently strong within a week or two to support body weight and assist in movement.

**Blood Pressure.**—Chart 1 shows a composite curve of the blood pressure levels of 5 dogs

for the first ten days, 4 dogs for the next twenty-nine days and 3 dogs for the next four days after section of the cord. Table 2 shows blood pres-

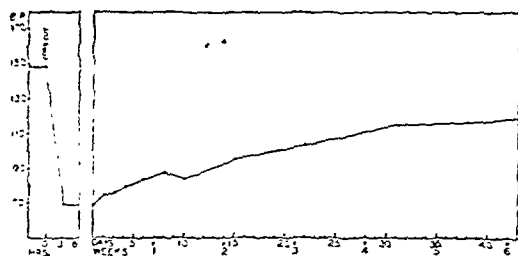


Chart 1.—Composite curve of blood pressures.

sure levels for the entire survival period of each animal of the group. These readings were recorded at the same time samples of blood were withdrawn. Although the blood pressure started rising by the end of the first week, the

TABLE 2.—Mean Blood Pressures of Five Dogs Following Experimental Section of the Spinal Cord at the Eighth Cervical Segment

Days After Section	Dog 234, Mm. Hg	Dog 302, Mm. Hg	Dog 234, Mm. Hg	Dog 237, Mm. Hg	Dog 238, Mm. Hg
Control.....	140	155	145	130	170
0-13.....	70	60	80	80	55
1.....	80	65	60	65	60
2.....	70	65	50	80	64
3.....	72	92	70	65	80
4.....	73	82	80	80	80
6.....	80	82	56	80	75
8.....	90	84	90	100	70
10.....	70	85	96	86	75
15.....	85	100	110	84	Killed 13th day
22.....	100	100	112	95	
29.....	...	105	120		
31.....	110	...	...	120	
35.....	...	...	122	116	
39.....	...	...	...	110	
42.....	115	...	...	Killed	
43.....	...	120	120		
56.....	...	120	138		
59.....	105				
71.....	...	120			
72.....	125				
73.....	...	...	125		
74.....	...	...	115		
77.....	...	125	Killed		
87.....	120	Killed			
119.....	150				
	Killed				

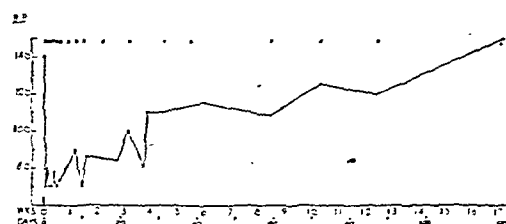


Chart 2. (dog 234).—Blood pressure curve during period of recovery.

which the pathologic report was osteosarcoma. Subsequent to this, fracture of the third metatarsal bone with callus formation developed. Excision was again requested, and the lesion proved to be benign march fracture with callus formation. Still later the patient had fractures of the first and fourth metatarsal bones, which were evident on roentgenographic examination. At the time the paper was written, he was living and working in a lumber mill fourteen years following operation on the second metatarsal bone. The specimen and the tissues were reexamined by Dr. Broders and showed unquestionably that the original lesion of the second metatarsal bone was osteosarcoma and that the lesion of the third metatarsal bone was march fracture.

Gershon-Cohen and Doran<sup>64</sup> review the literature of fatigue-stress fractures and emphasize the necessity for ruling out systemic disease and local pathologic changes. They support the hypothesis of fatigue-stress and present 4 cases. They state that the fracture lines are thin and the callus formation is diagnostic, although they believe that the lesion could be taken for osteogenic sarcoma in the latter stages of the condition.

[ED. NOTE.—My case reported at the beginning of this section illustrates the confusion which could arise by depending on roentgen interpretation alone.]

Friedman<sup>65</sup> reports a case of osteolytic osteogenic sarcoma of the os pubis, which is an extremely rare location. His patient was a woman 42 years of age. Roentgenographic examination revealed destruction of the right horizontal ramus of the pubic bone. The serum alkaline phosphatase was elevated to 18 units; the calcium and phosphorus levels were normal. A biopsy was done, and the pathologist's diagnosis was osteolytic osteogenic tumor of bone. Roentgen therapy was given for thirty-one months, with no essential change in the roentgenograms. The patient died of metastasis three and a half years later.

[ED. NOTE.—The very rare location of the lesion in this case, in which a thorough study of the microscopic and roentgenologic findings was made and the end result was obtained, makes reports of this type of value. My statistical studies of tumors of bone have been based on facts obtained from proved microscopic changes, histopathologic determination of the grade of malignancy and subsequent follow-up of cases.

Statistical reports without a report of the microscopic studies are not based on sufficient evidence of proof of malignancy and therefore are of less value in determining the benefits of treatment and prognosis than those based on microscopic studies.]

McNattin,<sup>66</sup> stimulated by the lack of satisfactory opinions concerning any one method of treatment of osteogenic sarcoma, reports a small series of cases in which the patients were treated by roentgen rays for from sixty to one hundred and forty treatments. The treatments were given over multiple portals, and amputation was done when the first signs of irradiation necrosis appeared. He believes that this form of therapy gives the best prognosis and that delay of amputation does not increase the likelihood of distant metastasis. He believes that if serial roentgenograms show some recession of the lesion, indicating radiosensitivity in this type of sarcoma, the total amount of irradiation may be decreased and amputation may be avoided.

[ED. NOTE.—Treatment by means of roentgen rays given preoperatively followed by amputation (Ferguson) delays removal of a malignant lesion. Such a delay is contrary to the common belief that early eradication is the method of choice. Unless there is microscopic proof of the grade of malignancy, I hardly feel that the results of treatment of osteogenic sarcoma by roentgen therapy alone are acceptable.]

Osteochondrosarcoma: Haggart, Hare and Marks<sup>67</sup> present a case in which osteochondrosarcoma arose from the rami of the pubis and ischium. The surgical removal of the tumor was made difficult by its location, since it was adjacent to and compressing the rectum.

Kemper and Bloom<sup>68</sup> present a case of osteochondrosarcoma. The patient was a girl, 13 years of age. Biopsy revealed a spindle cell osteochondrosarcoma of the right tibia without metastasis, and amputation through the lower part of the thigh was done. Two years subsequently there was an osteochondrosarcoma of the femur. At this time a midthigh amputation was done. Then about five months later a maxillary tumor, a mass in the upper right quadrant of the abdomen and recurrence of the osteochondrosar-

66. McNattin, R. F.: Treatment of Osteogenic Sarcoma with Preoperative Roentgen Radiation in Large Doses, *Radiology* 42:246-248 (March) 1944.

67. Haggart, G. F.; Hare, H. F., and Marks, J. H.: Clinico-Pathological Conference [Osteochondrosarcoma], *Radiology* 43:378-382 (Oct.) 1944.

68. Kemper, J. W., and Bloom, H. J.: Metastatic Osteochondroma of Maxilla from Primary Tumor of Tibia: Report of Case, *Am. J. Orthodontics (Oral Surg. Sect.)* 30:704-708 (Nov.) 1944.

64. Gershon-Cohen, J., and Doran, R. E.: Fatigue-Stress Fractures: Diverse Anatomic Location and Similarity to Malignant Lesions, *U. S. Nav. M. Bull.* 43: 674-684 (Oct.) 1944.

65. Friedman, S. T.: Osteogenic Osteolytic Sarcoma of the Os Pubis, *Am. J. Surg.* 64:248-253 (May) 1944.

curring secondarily in response to fluctuations in the concentration of total protein are necessary for the maintenance of normal calcium ion concentrations.<sup>3</sup> The values for serum potassium reached their highest levels after the sixth day following the operation and remained high until the dogs were killed.

*Cells.*—The following changes in the cell values were found to accompany the protein and electrolyte disturbances recorded in the serum: namely, an increased cell water content throughout the period; a distinct increase in potassium content in dog 234 throughout a period of eighty-seven days, with the highest values occurring

logic change found in any animal. No sections of tissue were taken for microscopic examination.

## COMMENT

To summarize the data for the 3 dogs, mean average concentrations were estimated for all constituents for the initial blood sample and for all experimental samples thereafter. The mean changes in per cent of the average initial concentration were plotted and are shown in chart 3 for serum and chart 4 for cells.

The period represented for four days on the curves is roughly the period of "spinal shock,"

TABLE 9.—Changes in Water, Electrolytes and Protein Concentrations (in per Cent of Control Values) in the Serum and Erythrocytes Following Experimental Section of the Spinal Cord at the Eighth Cervical Segment

Dog 233											
Serum											
Sample	Time After Section, Days	pH	Total CO <sub>2</sub> , mM	H <sub>2</sub> O, Gm.	Cl, mM	Na, mM	K, mM	Ca, mM	Mg, mM	Total Protein, Gm.	
Control	0	7.38	17.53	931.9	115.5	141.5	3.53	2.25	1.07	57.2	
			Δ %	Δ %	Δ %	Δ %	Δ %	Δ %	Δ %	Δ %	
2	0.15	-0.04	-14.15	+1.40	+ 3.29	+ 1.33	- 7.04	+ 9.78	+18.7	-11.20	
3	1	-0.07	-10.76	-1.35	- 3.03	+ 4.52	± 0	+ 6.22	+ 5.61	-12.40	
4	2	7.40	-13.40	+1.50	+ 5.64	+ 3.97	+ 5.45	- 5.34	+ 3.74	-22.90	
5	3	7.40	-20.10	+1.64	+ 2.60	- 4.31	+19.60	-11.10	+19.6	-23.09	
6	4	-0.11	+15.29	+1.72	- 3.64	- 2.71	+13.85	+10.21	.....	-20.10	
7	6	-0.07	+12.95	+1.01	- 3.21	- 1.60	+23.75	+ 7.56	+32.70	-10.50	
8	8	-0.05	+13.05	+0.97	- 0.26	+ 4.87	+56.90	+10.21	+10.28	- 0.87	
9	10	7.40	+ 4.13	+0.90	+ 3.28	- 1.46	+30.55	+ 4.44	+15.90	- 7.86	
Erythrocytes											
				Gm.	mM	mM	mM				
Control	0	.....	.....	695.0	53.0	100.3	11.96				
				Δ %	Δ %	Δ %	Δ %				
2	0.15	.....	.....	+1.82	+ 5.68	+ 0.40	+23.75				
3	1	.....	.....	+1.41	+64.6	+ 2.89	+21.00				
4	2	.....	.....	+0.14	+ 9.30	-13.05	+22.65				
5	3	.....	.....	+2.82	+13.10	-12.45	+23.10				
6	4	.....	.....	+3.24	+ 9.48	+25.80	-12.28				
7	6	.....	.....	+3.24	+ 1.35	+ 6.63	- 6.52				
8	8	.....	.....	+0.71	+ 9.48	+ 3.53	- 0.33				
9	10	.....	.....	-3.25	+ 9.83	+17.45	-10.65				

from the eighth to thirty-eighth day after operation, while in dog 237 the opposite, a decrease in the potassium content, was found, and a significant fall in the cell volume accompanied with a decreased oxygen content, the greatest and most constant decline occurring from the fourth to the fifteenth day following the cutting of the cord.

*Observations at Necropsy.*—In all animals the spinal cord was found to have been cleanly severed at the eighth cervical segment, and the cut ends were separated by fibrous tissue growth. A recent impaction in the lower bowel and thickening of the urinary bladder in dog 234 were the only gross evidences of visceral patho-

which has been discussed in the preceding paper. The days that follow are considered as the recovery period. Despite a relative constancy of serum water, the serum proteins increased from an average low value of 4.8 Gm. per hundred cubic centimeters on the fourth day to 5.4 Gm. per hundred cubic centimeters on the eighth day after operation. For fourteen days more the serum proteins remained at this low level, after which they returned gradually to normal. This fact indicates slight hemodilution, which may have been in part a result of the entrance of interstitial fluid into the blood stream from elsewhere in the body. This is evidenced by the slight gains in the serum water (0.5 to 1 per cent) and chloride (2 to 4 per cent) and the decreases in sodium (3 to 5 per cent). Fur-

3. McLean, F. C., and Hastings, A. B.: *Am. J. M. Sc.* 189:601, 1935.

and which later proved to be instances of primary carcinoma of the gastrointestinal tract.

[ED. NOTE.—We have had similar experience in a number of cases. The pathologist usually is able to suggest the probable primary location of the lesion.]

*I. Treatment.*—Phemister<sup>77</sup> discusses ununited fractures and defects of bone and feels that they may be satisfactorily repaired by transplantation of bone. In those instances in which an excision of bone was performed to eradicate a tumor (giant cell sarcoma, large benign tumors of bone, chondrosarcoma and so forth), the defect in the long bones was satisfactorily bridged by transplantation of bone.

[ED. NOTE.—I believe that low grade malignant lesions of bone, if recognized before they reach too great a size, and some benign lesions of bone and cysts of bone may be treated by excision and massive bone grafts with good results.]

Hormone and Castration Therapy in Carcinoma of Prostate and Breast: Middleton<sup>78</sup> reports a case of pathologic fracture with delayed union in the subtrochanteric region of the femur which healed after bilateral orchiectomy. The patient died twenty months subsequently, apparently from cerebral vascular accident.

Watkinson, Delory, King and Haddow<sup>79</sup> present 10 cases of carcinoma of the prostate, in 5 of which there was roentgenographic evidence of metastasis to bone. Improvement was noted in 9 cases following therapy with diethylstilbestrol.

Ritvo and Peterson<sup>80</sup> present cases in which the patients had metastasis of bone from carcinoma of the breast and in which regression, noted roentgenographically, was evident after ovarian sterilization. They believe that the regression results from the withdrawal of ovarian hormone. About a third or more of their patients had pronounced relief from pain and general physical improvement, with regression of the lesions of bone noticeable on roentgenographic examination.

[ED. NOTE.—The report of these 3 papers further illustrates the clinical benefits obtained when

patients with metastasis are treated by castration and administration of estrogens (diethylstilbestrol).]

*J. Experimental Studies of Primary and Secondary Tumors of Bone.*—Barrett, Dalton, Edwards and Greenstein<sup>81</sup> report on the history, cytologic and pathologic characteristics and phosphatase activity of a spontaneous, transplantable osteogenic sarcoma carried through eighteen generations of mice (at the time of writing). Early generations of subcutaneous transplants and pulmonary metastasis were osteogenic, with malignant osteoblasts, osteoid tissue and true bone. In later generations the character changed to a more rapidly growing anaplastic tumor which more closely resembled fibrosarcoma, and the capacity of the tumor to cause high alkaline phosphatase activity and to form osteoid tissue was lost or inhibited.

Dunlap, Aub, Evans and Harris<sup>82</sup> review some of the clinical and experimental work on ingestion and implantation of radium and radon in the production of osteogenic sarcoma. Thirteen male rats of the Wistar strain were given radium chloride for twenty days. Eight months subsequently, some objective signs of osteogenic sarcoma began to appear, and eventually osteogenic sarcoma developed in 9 of the 13 rats, with metastasis in 2. All tumor transplants except one failed because rats not of the Wistar strain were used. One transplant grew and since then has been successfully carried in about 50 per cent of attempts through seven serial generations in "Wistar" rats. The transplants have retained their original histologic characteristics and ability to form bone.

Abels and others<sup>83</sup> report that because heptyl-aldehyde bisulfite appeared toxic to human mammary carcinoma in vitro and produced liquefaction necrosis of spontaneous mammary carcinoma in mice they administered it to 14 women who had mammary carcinoma with metastasis to bone; it had no effect of any kind. They conclude that its in vitro effect is due to bisulfite which in vivo was hydrolyzed too rapidly to show any effect.

77. Phemister, D. B.: The Repair of Bone Defects and Ununited Fractures by Bone Transplantation, *Proc. Interst. Postgrad. M. A. North America* (1942), 1943, pp. 105-108.

78. Middleton, A. W.: Union of Pathologic Fracture of Femur Following Castrations for Carcinoma of Prostate, *Am. J. Surg.* 64:144-146 (April) 1944.

79. Watkinson, J. M.; Delory, G. E.; King, E. J., and Haddow, A.: Plasma Acid Phosphatase in Carcinoma of the Prostate and the Effect of Treatment with Stilboestrol, *Brit. M. J.* 2:492-495 (Oct. 14) 1944.

80. Ritvo, M., and Peterson, O. S., Jr.: Regression of Bone Metastases from Breast Cancer After Ovarian Sterilization, *Am. J. Roentgenol.* 51:220-229 (Feb.) 1944.

81. Barrett, M. K.; Dalton, A. J.; Edwards, J. E., and Greenstein, J. P.: Transplantable Osteogenic Sarcoma Originating in C<sub>3</sub>H Mouse, *J. Nat. Cancer Inst.* 4:389-402 (Feb.) 1944.

82. Dunlap, C. E.; Aub, J. C.; Evans, R. D., and Harris, R. S.: Transplantable Osteogenic Sarcomas Induced in Rats by Feeding Radium, *Am. J. Path.* 20: 1-21 (Jan.) 1944.

83. Abels, J. C.; Treves, N.; Herrmann, J.; Singher, H. O.; Kensler, C. J., and Rhoads, C. P.: The Administration of Heptyl-aldehyde Bisulfite to Patients with Inoperable Mammary Carcinoma Metastatic to Bone, *Cancer Research* 4:438-443 (July) 1944.



# FRAGMENTATION AND DISSOLUTION OF GALLSTONES BY CHLOROFORM

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CHICAGO

CICERO, ILL.

On certain occasions considerable difficulties arise during attempts to remove gallstones from the biliary tract. Calculi in the hepatic ducts found at the operation may tax the skill of a man with a wide experience in this type of work, not to speak of a general surgeon who encounters such conditions only once in a great while. W. Walters,<sup>1</sup> of the Mayo Clinic, cited a case in which he was not able to explore the intra-hepatic duct on account of a large, anomalous hepatic artery crossing the duct. Obesity of the patient may also interfere with exploration of the hepatic ducts. Inflammatory processes, edema and adhesions may further complicate the situation.

Some stones lodged in the common duct require a transduodenal approach or an extensive mobilization of the duodenum for exposure of the retroduodenal portion of the ductus choledochus. Both technical procedures, even in the hands of the more experienced surgeon, considerably increase the operative risk because of the danger of infection and hemorrhage, especially great in the presence of cholemia.

It is not surprising that because of such technical difficulties repeated attempts have been made to develop effective substitute procedures, with special attention to the problem of dissolution or fragmentation of gallstones by chemical means.

According to Naunyn's<sup>2</sup> classification, gallstones can be divided into four groups: (1) pure cholesterol stones; (2) pure pigment-calcium, or "mulberry," stones (the pigment may be either bilirubin or biliverdin); (3) mixed calculi consisting mainly of cholesterol, calcium bilirubinate and calcium carbonate, and (4) pure calcium carbonate stones. The last group can

be disregarded for the purposes of this study because stones of this type are found mostly in animals and rarely in man.

Inasmuch as in many instances the character of the stone cannot be determined in the course of the operation, a desirable solvent would be one which acts on both cholesterol and pigment. Calcium and also the binding mucoid substances which serve as the organic framework for the precipitated elements of the bile are reduced to a soft pulp which can be easily washed out by bile flow after a fragmentation of the stones has been accomplished.

Obviously the substance employed for this purpose must meet two requirements: It must have a strong solvent action on the stones, and it must be innocuous for the living tissues.

Attempts to find a suitable substance have been made repeatedly. In 1901 Walker<sup>3</sup> cited a case in which he used an ether-glycerin mixture to dissolve a stone by irrigation through a biliary fistula. Wright<sup>4</sup> reported a case in which a stone impacted in the common duct could be removed only after injection of turpentine. Pribram<sup>5</sup> recommended daily injections of ether through a T tube in cases in which a stone is firmly lodged in the papilla or in which the least suspicion exists that all the concrements have not been removed. He noticed that unless the tube is left open after the injection has been completed epigastric distress results from the vaporization of the ether, which takes place at body temperature. Walters and Wesson<sup>1</sup> obtained a fragmentation of a stone with injections of ethyl ether on three successive days and two subsequent injections of a solution consisting of one-third ethyl alcohol and two-thirds ethyl ether, as suggested by Osterberg. However, nausea and severe pain in the right upper quadrant of

Dr. Warren H. Cole made valuable suggestions in the preparation of this paper and granted us the privilege of performing the experiments in the laboratory of the department of surgery, University of Illinois College of Medicine.

1. Walters, W., and Wesson, H. R.: Fragmentation and Expulsion of a Common Duct Stone into the Duodenum Using Ether and Amyl Nitrite: Preliminary Report, Proc. Staff Meet., Mayo Clin. 12:260, 1937.

2. Naunyn, cited by Darling, H. C.: Cholelithiasis (Latent and Active), M. J. Australia 2:555, 1941.

3. Walker, cited by Raffi, A. B.: Experimental Studies on the Solvent Action of Ether on Gallstones, Am. J. Surg. 52:65, 1941.

4. Wright, G.: The Value of Turpentine in Gallstone Operations, Brit. M. J. 2:1808, 1908.

5. Pribram, B. C.: Zur Beseitigung eingeklemmter Choledochuspapillensteine, Deutsche med. Wchnschr. 58: 1167, 1932; New Methods in Gallstone Surgery, Surg., Gynec. & Obst. 60:55, 1935.

esses and strains. In coxa valga, the internal architecture undergoes a devolutionary change as a result of modification of the external form and similar to that of the almost straight reptilian fur. In osteoarthritis, a new compact articular face is formed superficial to the original one and supported by new trabeculated elements which continue the radiating lines of the original trabecular pattern. A devolutionary process, which in the external architecture and consequently in the internal architecture, takes place in the femurs of the amputated femurs after loss of the normal function of weight bearing. In 2 specimens examined after amputation, there was an increase in the neck angle, a decrease in the length of the neck and displacement of the head of the femur laterally, backward and downward. The backward displacement represented a return of the head on the neck and exposed the medial part of the anterior surface of the neck to pressure of the iliofemoral ligament and the anterior margin of the acetabulum, thus producing extension of the articular surface of the head in this region.

Kleinberg<sup>89</sup> reports a case of aseptic necrosis of the femoral head following a dislocation which he believes was not associated with a tear of the round ligament. Exploration of the hip showed a normal-appearing ligamentum teres, grossly and microscopically. He believes that this case demonstrates that rupture of the ligamentum teres is not a constant occurrence in a traumatic dislocation. The author points out that in most cases in which the femoral head is deliberately dislocated from the acetabulum the round ligament is torn. It is not infrequently the head can be removed from the acetabulum without rupturing the round ligament.

Salmore<sup>90</sup> measured the pelvifemoral angle in 100 normal persons and found that the most accurate measurements could be made with the patient in the erect position. This angle was defined by Milch as the backward opening angle formed by the axis of the femoral shaft with Delatton's line; it is valuable in measuring the degree of hip flexion. It was found to be between 0 and 52 degrees in normal adults and children and 58 degrees in the preambulatory infant.

Wellmerling<sup>91</sup> discusses the management of fractures of the femoral neck in relation to certain anatomic considerations of the upper end of

the femur. There are two distinct systems of trabeculae arranged in curved paths, one beginning on the medial side of the upper femoral shaft and curving upward in a fanlike radiation to the opposite portion of the bone and the other originating in the lateral portion of the upper shaft, arching upward and medially. The result of the dense converging trabeculae is a thickened anterior and medial cortex. The fracture is reduced by overtraction in adduction and fixed in a coxa valga position, thereby interlocking the fragments and restoring the normal length. The author relies on his senses and insertion of a guide wire and cannulated nail, controlled by two plane roentgenography, rather than directing devices. For fixation he uses a 5 inch (12.7 cm.) cannulated, vitallium Smith-Peterson nail. The cortex is entered just posterior to the center of the lateral aspect of the shaft and 2 inches (5 cm.) distal to the distal prominence of the trochanter with a 5/32 inch (0.4 cm.) drill. The nail is driven with a 20 degree forward inclination so that it lies in the anteromedial wall of the neck, where the converging trabeculae are the most supportive. If the nail enters the midportion or anterior to it, the nail will emerge through the anterior portion of the neck. [Ed. NOTE.—In cases of oblique neck fractures with a spicule beneath the proximal fragment, abduction is usually necessary to accomplish reduction.]

Siris and Ryan<sup>92</sup> believe that the chances of survival are better in cases of intracapsular fractures of the neck of the femur when reduction is done immediately. The use of two machines has simplified the technic and makes draping easier. They do not permit the patients to turn on the uninjured side, because in a certain number of cases this has caused loosening of the nail.

Miller and Bishop<sup>93</sup> reported the case of a 76 year old patient with a fracture of the femoral neck, who died during manipulation of the hip while he was under cyclopropane anesthesia eighteen days following fracture. Autopsy revealed a pulmonary embolism which came from the femoral vein. The authors suggest that early reduction might reduce the incidence of this complication.

Weinberger<sup>94</sup> describes a method for converting fractures of the femoral neck into a valgus

89. Kleinberg, S.: Aseptic Necrosis of the Head of the Femur Following Dislocation of Hip, *Arch. Surg.* 9:104-108 (Aug.) 1944.

90. Salmore, W.: Pelvifemoral Angle, *J. Bone & Joint Surg.* 26:392-393 (April) 1944.

91. Wellmerling, H. W.: New Therapy of Hip-fracturing: Precision Technique for Intracapsular Fractures, *Indust. Med.* 13:809-817 (Oct.) 1944.

92. Siris, I. E., and Ryan, J. D.: Fractures of the Neck of the Femur: An Analysis of 157 Intracapsular and Extracapsular Fractures, *Surg., Gynec. & Obst.* 78:631-639 (June) 1944.

93. Miller, S., and Bishop, H. F.: Fatal Pulmonary Embolism During Manipulation of Hip Under Anesthesia, *Anesthesiology* 5:300-302 (May) 1944.

94. Weinberger, M.: Modification of Lines of Force in Treating Fractures of Neck, *Rev. brasil. de ortop. e traumatol.* 4:235-240 (Sept.-Dec.) 1943.

# CLEANSING OF OIL-COVERED SKIN AND BURNS

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In this investigation a survey of the effectiveness of surface-active agents for the removal of heavy oils and tars from intact and from injured skin has been carried out. At the present time, a large number of surface-active agents are commercially available. These many compounds and mixtures have in common the power to modify the properties of surfaces but vary widely in specific modes of surface activity, such as wetting power, emulsifying power, and dispersing, penetrating and foaming action, not only with respect to any specific system of surfaces but also from one system to another.

If the living skin is considered a component of such a system of surfaces, the pertinent powers of surface-active agents may in general be taken to vary between wetting power, on the one hand, and emulsifying power, on the other, although these do not necessarily oppose each other. The former is a measure of the ability of a compound to lower interfacial tension; the latter, a measure of ability of a compound to prevent the breaking of an emulsion. The dermatologically important property of detergency is a combination of these powers and is not necessarily parallel to either. Sodium dioctylsulfosuccinate (Aerosol OT) is an excellent wetting agent but not so good an emulsifying agent. Sodium kerylbenzenesulfonate (Nacconol) is both a good wetting agent and a good detergent, while the cation-active invert soap cetyldimethylbenzylammonium chloride (Triton K-60) is an excellent emulsifying agent but of limited powers as a wetting agent or as a detergent. Sodium lauryl sulfate (Duponol) is an excellent detergent and a fair wetting agent; sodium stearate (common soap) is a poor wetting agent but an excellent detergent. In any case, it is evident that "detergent" is too general a term for the substances involved. They are better classified as "surface-active agents," and at present they may be regarded as falling

into the following chemical types (for a more complete review of this topic, see Snell<sup>1</sup>).

1. Alkali salts of long chain fatty acids, e. g., ordinary soap.\*

2. Alkali salts of sulfated long chain fatty alcohols (e. g., sodium lauryl sulfate, Duponol), esters (e. g., sodium glyceryltriricinoleate sulfate, sulfated castor oil) and amides (e. g., sodium N-oleyl taurate, Igepon T).

3. Alkali salts of long chain fatty sulfonic acids (e. g., sodium petroleum sulfonate, SP 315).

4. Alkali salts of alkylaryl sulfonates (e. g., sodium kerylbenzenesulfonate, Nacconol).

5. Polymerized ethers, esters and alcohols (e. g., the polyoxyalkylene ether of partial lauric acid esters, Tween).

6. Acid salts of quaternary ammonium bases, cation-active "invert soaps" (e. g., cetyldimethylbenzylammonium chloride, Triton K-60).

The specific requirements of any instance in which surface-active agents are to be used thus should dictate which special set of properties is to be sought. In this study an attempt has been made to determine which surface-active agent or agents and in what forms would best serve to remove heavy oils and tars from intact and from damaged skin. All the products listed in a compilation appearing in the January 1943 issue of *Industrial and Engineering Chemistry*, entitled "Surface-Active Agents Manufactured in the United States and Commercially Available," were requested from their manufacturers. Those received, together with some common surface-active agents not listed and some of those recently developed but not listed, were submitted to test. These totaled one hundred and sixty-five substances, and each was tested in a variety of forms and according to several criteria of excellence.

Initial results corroborated those reported by Rosenberg<sup>2</sup> and Schwartz<sup>3</sup>: When light oils con-

1. Snell, F. D.: *Indust. & Engin. Chem.* **35**:107, 1943.

2. Rosenberg, N.: *Surgery* **13**:385, 1943.

3. Schwartz, L.: *Pub. Health Rep.* **56**:1788, 1941.

From the Dermatoses Section, Industrial Hygiene Division, Bureau of State Services.

duration of hospitalization was shortened. Since the authors adopted the use of a Steinmann pin through the lower part of the femur and the incorporation of the pin in the cast, as suggested by Key, the complications of pressure sores and foot drop have been eliminated. The cast is now applied with the knee in 30 to 40 degrees flexion, with plaster loops on the anterolateral aspect, incorporated at the knee and foot for traction. One to three days later the patient is placed in a wheel chair with a pillow beneath the cast, and the foot-board is turned up, so that the legs hang without support. Crutches may be used in three weeks. The cast is removed after an average of forty-three and four-tenths days and the patient discharged on crutches. Complications, such as pneumonia, decubitus ulcer, stiffness of knees and ankles and weakness from lying in bed are reduced. The reductions have been found to be as good as those obtained with other methods, and nonunion has not occurred. [ED. NOTE (J. J. F.).—This method is novel in the management of these fractures and demands careful consideration. Immobilization with plaster would be expected to cause more articular stiffness than the methods now employed.]

Pascau, Ponce de Leon and Aymerich<sup>100</sup> obtained bony union in 55 of 59 cases of trochanteric fractures treated by traction with a Kirschner wire through the supracondylar portion of the femur. Fifty-one of these patients recovered complete function. Only 2 had a coxa vara deformity. [ED. NOTE (J. J. F.).—The recovery of function of the knee following traction in this age group is usually slow, and not uncommonly some permanent limitation of motion results. The incidence of coxa vara reported in this paper is unusually low, as compared with that in other reports.]

Leadbetter<sup>101</sup> describes an osteotomy high in the cervical axis which is accomplished under full vision and avoids the ascending ramus of the femoral nutrient artery as well as the cervical branches of the circumflex femoral artery. The apposition of abundant cancellous bone is established, with positive pressure beneath the capital portion of the bone in a true valgus position. The osteotomy is made through an anterior approach. The capsule is opened by a cruciate or a semilunar incision, and any comminuted or projecting fragments at the lower part of the head are

removed. The osteotomy is done in the long axis at the junction of its middle and upper thirds, and the neck is then displaced beneath the head to a point within the lower acetabular rim. During the fourth week, the plaster is bivalved and massage and quadriceps-setting exercises begin; the plaster is removed in eight weeks. Eight patients were operated on and observed for at least one year. Every patient had a functioning and weight-bearing hip, and solid union occurred in 6. [ED. NOTE (J. J. F.).—This operation seems promising. Its value will be more accurately determined when more cases are reported. The early quadriceps exercises help to reduce the disability caused by stiffness of the joint.]

Schneider<sup>102</sup> discusses nonunion of the femoral neck and the difficulties encountered with the various present day methods of treatment. He has not found the Blount blade plate fixation for osteotomy, performed for nonunion, to be the entire answer, as in some cases the plate will pull out anteriorly as the extremity goes into external rotation or the screws loosen from the atrophic bone. The Smith-Peterson nail with the Thornton plate has been more satisfactory in his hands, but this method does not always suffice unaided by external support. [ED. NOTE (J. J. F.).—This complication is not as frequent when the plate is introduced in the location used for internal fixation as it is when the plate is introduced high in the trochanteric cancellous bone.]

Rowe and Ghormley<sup>103</sup> state that while most authors believe that bone grafting yields the best end results in the treatment of nonunion of the femoral neck it is well known that only a small percentage of the cases meet the indications for this operation. While many have expressed the opinion that osteotomy offers the simplest and safest procedure for the patient who presents a poor risk and the ones not suitable for osteosynthesis, the authors believe that better mechanical function can be attained by the use of one of the reconstructive operations if the condition of the patient does not prohibit it. If the head is nonviable, the Whitman, the Cplonna or the Albee procedure is indicated. If the head is viable and the degree of absorption rules out a bone-grafting procedure, then the Brackett operation is indicated. A single long vitallium screw, fix-

100. Pascau, I.; Ponce de Leon, A., and Aymerich, E.: Nonsurgical Therapy of Fractures of the Trochanteric Region, *Cir. ortop. y traumatol.*, Habana **11**:19-29 (Jan.-June) 1943.

101. Leadbetter, G. W.: Cervical-Axial Osteotomy of Femur: A Preliminary Report, *J. Bone & Joint Surg.* **26**:713-720 (Oct.) 1944.

102. Schneider, C. C.: *Sequelae of Fractures of Neck of Femur and Their Treatment*, Wisconsin M. J. **43**:799-804 (Aug.) 1944.

103. Rowe, M. L., and Ghormley, R. K.: Brackett Operation for Ununited Fractures of the Neck of the Femur, *J. Bone & Joint Surg.* **26**:249-256 (April) 1944.

# NITROGEN BALANCE STUDIES ON SURGICAL PATIENTS RECEIVING AMINO ACIDS

OBSERVATIONS ON PATIENTS WITH OBSTRUCTING LESIONS OF THE ESOPHAGUS AND  
STOMACH RECEIVING AMINO ACIDS BY PARENTERAL INJECTIONS  
AS THE EXCLUSIVE SOURCE OF PROTEIN

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In the six years that have elapsed since Elman and Weiner<sup>1</sup> first succeeded in giving amino acids intravenously to human beings, the parenteral administration of amino acids in the form of specially prepared protein hydrolysates has become an established clinical procedure. This has been particularly true in the management of cases of gastrointestinal diseases in which the existence of protein deficiency is usually easily recognized and in which the possibility of oral alimentation is limited or impossible. At first glance the nutritional value of such a method of feeding would appear obvious. However, many factors are involved in its successful application. Even though the products available for parenteral use are derived from nutritionally good proteins, it is not safe to assume them to be adequate until they are proved by proper studies under controlled conditions to be able to provide nitrogen balance. Also, it is necessary to recognize the quantities of amino acids needed for the particular patient, the adjuvant requirements of carbohydrate, minerals and vitamins, the best method of administration and the limitations of the efficacy of such management even under the best of conditions. The present report is a part of an investigation to determine some of these factors.

## PLAN OF STUDY

To study the adequacy of therapy with parenteral injections of amino acid, a series of cases of obstructive lesions of the esophagus and stomach was chosen.

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From the Hektoen Institute for Medical Research of the Cook County Hospital, the Department of Surgery of the Cook County Hospital and the Cook County Graduate School of Medicine, and the Department of Surgery, Northwestern University Medical School.

1. Elman, R., and Weiner, D. O.: Intravenous Alimentation with Special Reference to Protein (Amino Acid) Metabolism, *J. A. M. A.* **112**:796 (March 4) 1939.

This type of case presents a severe nutritional challenge to the clinician. The patients were predominantly men of 50 years or older, unable to eat solid food for weeks or months and often unable to retain liquids. Their teeth and gums were in poor condition. Because of frequent vomiting, many of them were considerably dehydrated. Their fat stores were for the most part depleted. The average loss in weight was 36 pounds (16.3 Kg.). More than 40 per cent of these patients had secondary anemia on admission to the hospital. In others the anemia became manifest after fluid and salt had been administered. The incidence of hypoproteinemia in these patients was 50 per cent, much higher than the 23 per cent reported from this institution<sup>2</sup> for the general variety of patients with surgical lesions. Here, again, the incidence would probably have been still higher if it had been redetermined after hemoconcentration had been eradicated by administration of fluid and salt. That such patients do not tolerate operations well has been fully demonstrated in a review of 80 cases of gastrostomy performed at the Cook County Hospital between 1941 and 1944.<sup>3</sup> Of the 80 patients operated on, 43 died within two months, a good portion of these during the first week. The nutritional status of such patients is difficult to improve unless one resorts to parenteral feeding. The clinical evaluation of the results of such a nutritional program instituted for them is likely to be unequivocal. Also, since the intake of amino acids can be accurately determined and since the number of stools to be analyzed is small, it is relatively easy to make accurate nitrogen balance studies on these patients in surgical wards.

Nitrogen balance studies conducted in this series of cases permit the evaluation of the adequacy of the amino acid preparations used, for if any of the essential amino acids are not present in sufficient amounts a positive nitrogen balance will not be obtained except with extraordinarily large quantities of the preparation.<sup>4</sup> Furthermore, they allow the recognition of the

2. Meyer, K. A., and Kozoll, D. D.: Protein Deficiency in Surgical Patients, *Surg., Gynec. & Obst.* **78**: 181, 1944.

3. Meyer, K. A., and Kozoll, D. D.: Gastrostomy, *Surg., Gynec. & Obst.* **81**:221, 1945.

4. Rose, W. C.; Haines, W. J., and Johnson, J. E.: The Role of the Amino Acids in Human Nutrition, *J. Biol. Chem.* **146**:683, 1942. Holt, L. E., Jr.; Albanese, A. A.; Brumback, J. E., Jr.; Kajdi, C., and Wangerin, D. M.: Nitrogen Balance in Experimental Tryptophane Deficiency in Man, *Proc. Soc. Exper. Biol. & Med.* **48**:726, 1941.

are not usually willing to accept it, and it is contraindicated when both hips are involved and when the spine is affected. Cup arthroplasty may offer hope of retaining motion and relieving pain in certain cases.

Bergmann<sup>110</sup> discusses aseptic bone necrosis in lesions of the hip. In fractures of the femoral neck, the arteries running along the inner lining of the capsule and entering the head are destroyed, leaving only the vessels of the round ligament, which are insufficient in most instances to keep the head from undergoing necrosis. The adjacent living bone of the distal fragment unites with the head before it has gone through all the stages of reorganization. The endosteum of the distal fragment is the only source from which new bone is laid down, and this is inferior to periosteal callus. The pathologic changes of Perthes' disease (osteochondrosis of the capital epiphysis of the femur), congenital dislocation of the hip and caisson disease are discussed and illustrated with roentgenograms and photographs. [ED. NOTE (J. J. F.).—One interested in the pathologic changes of aseptic necrosis of the head of the femur should read this well illustrated article. In fractures of the femoral neck, there often remains a significant blood supply from the posterior capsular vessels.]

Stephens<sup>111</sup> reviews the literature on iliopsoas bursa and adds 2 cases to the literature. The globular mass may be confused with an enlarged inguinal node or a femoral hernia. Aspiration of seromucous fluid will differentiate it from the former, and pulsation on top of the tumor will distinguish it from the latter. A psoas abscess is more fluctuant. Unilateral chronic disease of the hip joint on the involved side suggests a possible associated bursitis. The simplest method of treatment is aspiration followed by administration of sclerosing solutions. If suppuration occurs, incision and packing are advocated.

Pusitz<sup>112</sup> believes that serious gunshot wounds of the hip and buttock with much fragmentation of the head, seen late, are best treated by resection of the femoral head, sulfonamide compounds and Orr's treatment. A reconstruction or arthrodesis may be performed subsequent to the control of the infection. In cases in which there is much destruction of tissue and in which a portion of

the sciatic nerve is lost, débridement removal of bone and, later, disarticulation of the hip may be indicated. One such case is reported in detail.

Watson and Berkman<sup>113</sup> state that failure to recognize march fractures of the femoral neck promptly may result in serious disability and deformity. They report the case of a soldier 34 years old who experienced sudden severe pain in his hip while hiking and a few days later had pain on the inner side of his thigh and knee. He continued activity, and one month later roentgenograms showed an incomplete fracture with shortening and limited motion of the hip. He was treated by traction for two weeks and then used crutches, without weight bearing, for four months.

Harmon and Adams<sup>114</sup> review the end results of surgical reconstruction in 53 patients who previously had had acute pyogenic arthritis. Chronically discharging sinuses responded satisfactorily to treatment in 80 per cent of the cases. Positional correction of an ankylosed hip, ankylosis of a painful hip and certain plastic procedures performed on young persons were found to be more satisfactory than arthroplastic procedures. Excision of the major part of the ilium in certain cases was thought to be of value when this portion of the pelvis was affected. Disarticulation of the hip joint should receive more consideration in the treatment of persistent suppuration of the hip joint in adults in the presence of osteomyelitis in the upper half of the femur. For young persons with unilateral instability of the hip joint the shelf operation is the procedure of choice, while for adults surgical arthrodesis is performed at the level of the acetabulum after the replacement of the dislocated hip. [ED. NOTE (J. J. F.).—This article is well illustrated and many data are tabulated. Interested persons should refer to the original.]

Milch<sup>115</sup> is of the opinion that the angle of abduction is an unsatisfactory guide in performing an upper femoral osteotomy, and the post-osteotomy angle is suggested instead. This angle represents the angle of the neck of the osteotomized femur and is measured by the line of the shaft and the line running from the upper end of the osteotomized shaft to the femoral neck.

113. Watson, F. C., and Berkman, E. F.: Fatigue (March) Fractures of Femoral Neck, *J. Bone & Joint Surg.* 26:404-405 (April) 1944.

114. Harmon, P. H., and Adams, C. O.: Pyogenic Coxitis: Indications for Surgical Treatment in Residual and Chronic Stages and End Results of Reconstruction in Fifty-Three Patients, *Surg., Gynec. & Obst.* 78:497-508 (May) 1944.

115. Milch, H.: The Postosteotomy Angle, *J. Bone & Joint Surg.* 26:394-400 (April) 1944.

110. Bergmann, E.: Role of Aseptic Bone Necrosis in Hip Lesions, *Am. J. Surg.* 63:218-235 (Feb.) 1944.

111. Stephens, V. R.: Tumor of Iliopsoas Bursa: Two Cases, *Arch. Surg.* 49:9-11 (July) 1944.

112. Pusitz, M. E., and Taylor, R. M.: Serious Gunshot Wounds of Hip, *J. Kansas M. Soc.* 44:397-400 (Dec.) 1943.

pleasant sense of fullness, as after a full meal. But this lasted only for an hour or two. If vomiting preceded therapy, it usually abated after a few days of amino acid therapy and the patient expressed a desire for oral feeding. Subcutaneous and intrasternal infusions were not tolerated so well as intravenous injection, because of local pain. However, in no case was there any slough or other sign of local damage. Intragastric feeding through a gastrostomy opening was also successful, as was transgastric feeding immediately postoperatively through an Abbott-Rawson tube.

The daily nitrogen excretion in the control periods ranged from 2.25 to 10.4 Gm., the average being 6 Gm. While this average value

intake. In those cases in which 200 to 300 Gm. of carbohydrate was furnished, there was indeed a tendency toward low nitrogen excretion. In the cases in which there were higher excretions, factors other than inadequate intake of carbohydrate or the lack of fat stores were probably also operative, such as excessive breakdown of tissue due to carcinoma.

The results shown in the table indicate that positive nitrogen balance can be achieved with parenteral administration of both Parenamine and Cutter's amino acids as the only source of nitrogen. In only 1 case was there a complete failure to achieve positive balance during any period (case 4). In this case, even 135 Gm. of Parenamine and 200 to 250 Gm. of carbohydrate daily

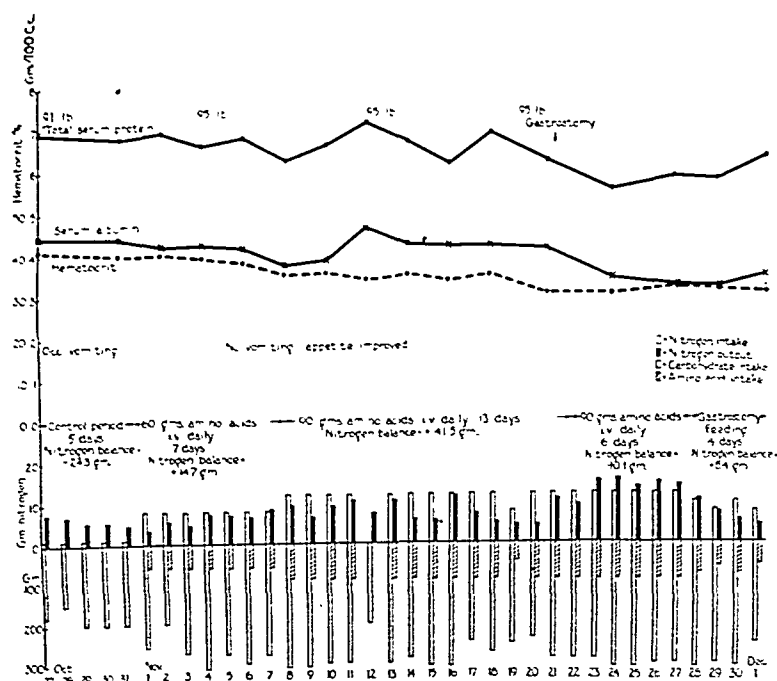


Fig. 5 (case 5).—Nitrogen balance study in a case of carcinoma of the esophagus with loss of 4.85 Gm. of nitrogen per day with a serum protein level of 6.9 Gm. per hundred cubic centimeters, serum albumin level of 4.4 Gm. and a hematocrit value of 41 per cent. When 60 Gm. of amino acids (Parenamine) was given intravenously per day, a positive nitrogen balance of 2.1 Gm. per day occurred, with a gain in weight of 4 pounds (1.8 Kg.). The serum proteins fell to 6.2 Gm. per hundred cubic centimeters, the serum albumin to 3.8 Gm. and the hematocrit value to 35 per cent. On 90 Gm. per day, a positive nitrogen balance of 3.2 Gm. per day resulted, with a restoration of serum albumin. The same quantity of amino acids postoperatively produced a negative nitrogen balance of 1.6 Gm. per day with a drop in serum protein and albumin, which is slight in comparison with usual nitrogen losses following surgical treatment. A positive nitrogen balance of 2.1 Gm. per day was also achieved when the amino acids were administered in gastrostomy feedings.

is of the order usually obtained in starvation, it is probably a coincidence, for there were 3 cases of unusually low excretion, 2 to 3 Gm. daily, and 2 of rather large excretions, 10 Gm. daily. Subjects who have lost a great deal of weight would be expected to show a minimal nitrogen excretion (2 to 3 Gm. per day) if their fat stores were plentiful and if at least 50 per cent of their caloric requirements were met by carbohydrate

were inadequate. In other cases (cases 3, 6, 7 and 11) a negative nitrogen balance on 60 Gm. of amino acids gave way to a positive balance when 90 to 120 Gm. was used. In still others (cases 1, 2, 5, 8 and 9) 60 Gm. was sufficient to produce at least a modest positive nitrogen balance. This lack of consistency in the requirements of amino acids for positive nitrogen balance would signify that in these cases it was a

weight bearing is delayed until the dead bone has been replaced. Vitallium cup arthroplasty may offer favorable results in certain cases complicated by traumatic arthritis and aseptic necrosis. [Ed. NOTE (L. D. B.).—This report should be compared with that of Bickel and Ghormley.<sup>116</sup> The most disappointing results were obtained when operation was performed for aseptic necrosis.]

#### V. CONDITIONS INVOLVING THE FOOT AND ANKLE

EMIL D. W. HAUSER, M.D., CHICAGO, AND ROBERT P. MONTGOMERY, M.D., MILWAUKEE

Dew and Wooten<sup>122</sup> present a series of 58 march fractures of the metatarsal bones involving 55 trainees. The majority of patients failed to disclose any preexisting pathologic condition of the feet. March fractures are attributable to the carrying of heavy full field equipment and marching of distances longer than 6 miles (9.6 km.) on a hard surfaced road. Local treatment of mild fractures consists in the use of an ice bag for seventy-two hours, a whirlpool bag, a daily massage and crutches; moderate weight bearing within pain limit is allowed. Splinting of any form is not advised because of the ensuing stiffness of the foot and the increasing morbidity. The prophylactic measures advanced by the authors have materially lowered the high incidences of march fracture. They recommend gradual lengthening of the march, progressive increase of field equipment and, what is most important, marching on the soft shoulders of the roads or across the fields.

Krause and Thompson<sup>123</sup> report the results of a study of 200 soldiers who sustained 220 march fractures of the metatarsals between May 1941 and August 1943. Special attention is given to possible predisposing factors, and the various theories which have been advanced to explain the pathogenesis of these fractures are discussed. The immediate cause of the fracture is the rhythmically repeated, subthreshold traumas incident to marching, which, acting by summation, reach a point beyond the ability of the bone to bear stress. Fatigue of the calf muscle causes these subthreshold injuries to be accentuated. The clinical observations and roentgenologic appearances are described in detail. Conservative treatment restores these men to duty with a minimum of time lost.

Wolin<sup>121</sup> describes the case of a man with a Charcot joint who was treated for a dislocation of the hip following a fall; shortly after treatment the dislocation recurred. Roentgenograms showed nothing abnormal, except for the dislocation, until one year later, when a fracture with disorganization of the femoral head was found.

121. Wolin, I.: Tabetic Arthropathy of Hip, *Radiology* 42:79-80 (Jan.) 1944.

In a study of a series of 82 cases of march fracture, Kernodle and Jacobs<sup>124</sup> felt that physiologic inadequacy of these feet was a factor even in their series, although they could not demonstrate any gross mechanical inadequacy. The fatigue element with loss of elasticity of the foot has been observed repeatedly and would expose the bony elements to more direct strain. The authors mention a suggestion that march fracture is based on the torsion mechanics of the foot and is due to an acute sinking of a previously well formed foot. Under stress, the medial portion of the anterior part of the foot gives way, and weight bearing is shifted to the second and third metatarsals, which become traumatized and may ultimately break down.

The treatment is varied according to the stage of the fracture when seen. If the period is less than two weeks, a short leg cast molded under the metatarsal heads is applied and a walking rubber attached for a period of three to four weeks, followed by physical therapy for a week, and a metatarsal sponge pad is worn in the shoe. If the time is three to five weeks and there is moderate callus formation, simple pads and physical therapy with moderate rest suffice.

Tyner and Hileman<sup>125</sup> studied 166 cases of march fracture, securing accurate information as to the time the fracture occurred after the beginning of the march, the foot involved and the metatarsal involved. The blood chemistry was studied in 12 cases. Three cases are reported in detail. They believe that the most important factor in the production of these fractures is the increased stress on the metatarsal bones, induced by muscular fatigue.

According to Breck and Higinbotham,<sup>126</sup> march fractures are felt to be due to crystalliza-

122. Dew, W. A., and Wooten, J. H., Jr.: March Fractures: A Series of Fifty-Eight, *Mil. Surgeon* 95: 356-359 (Nov.) 1944.

123. Krause, G. R., and Thompson, J. R., Jr.: March Fracture: An Analysis of Two Hundred Cases, *Am. J. Roentgenol.* 52:281-290 (Sept.) 1944.

124. Kernodle, H. B., and Jacobs, J. E.: Metatarsal March Fractures, *South. M. J.* 37:579-582 (Oct.) 1944.

125. Tyner, F. H., and Hileman, W. T.: March Fractures: An Analysis of One Hundred and Sixty-Six Cases, *Am. J. Roentgenol.* 52:165-172 (Aug.) 1944.

(Footnotes continued on next page)



The severity of the protein deficiency in a group of patients such as those studied here can be determined in another way. The average loss of weight was 16 Kg. It is of course impossible to determine the distribution of that loss in terms of water, protein and fat. But if one assumes that such patients show a relationship of nitrogen loss of weight corresponding to that found by Ask<sup>21</sup> in the study of undernourished persons—it is, 30 Gm. of nitrogen for each kilogram of body weight lost—then these patients have lost out 480 Gm. of nitrogen. A daily positive nitrogen balance of 4 Gm. would be required for one hundred and twenty days to restore the lost protein.

3. The gain in nitrogen may be used up in the growth of metastases. In the patients with rapidly metastasizing carcinomas, positive nitrogen balance was not difficult to achieve. Their urinary nitrogen excretion was small and that of the feces negligible. There was no elevation of the blood nonprotein nitrogen. Yet these patients, in spite of good positive nitrogen balances, not only showed no clinical improvement but manifested a precipitous drop in serum protein too great to be accounted for by the simultaneous hemodilution. Since at autopsy extensive formation of new tissue as metastases was observed, it is possible that the increase in the growth of the neoplasm utilizes the available nitrogen at the expense of the plasma proteins, even in the face of a positive nitrogen balance. Such a phenomenon is consistent with the recent observations of White and Belkin<sup>22</sup> that tumor transplants in rats grow rapidly in spite of negative nitrogen balances associated with a low protein diet, apparently at the expense of the tissues of the host.

4. The albumin-making mechanisms, which are believed to be found chiefly in the liver, may be damaged enough to prevent a rise in serum albumin. To this phenomenon has generally been attributed the fall of serum albumin in cirrhosis of the liver, though it should be recognized that the continued production of serum protein in cirrhosis in spite of the repeated removal of large quantities by paracentesis would indicate, on the contrary, a stimulation of albumin production similar to that seen in the plasmapheresis experiment in dogs by Whipple

and his co-workers.<sup>23</sup> However, low serum protein concentrations are not infrequently encountered in cases of cirrhosis without ascites, and it may be that cases of carcinoma with extensive metastases to the liver are similarly involved. Furthermore, there is the possibility that severe protein deficiency itself is capable of undermining the ability of the liver to manufacture albumin, even when furnished with an adequate supply of amino acids. If such were the case, a rise in serum protein level might not occur until the liver itself has been restored.

Available data on the blood concentrations and urinary excretions of amino acid nitrogen, phosphate, sulfate, urea and creatinine have been omitted as not being pertinent to the main thesis of this paper. It can be stated that the morning plasma levels of amino acid nitrogen during the whole treatment ranged between 3 and 8 mg. per hundred cubic centimeters, as in normal persons. The daily urinary excretion of amino acid nitrogen ranged from 0.2 to 0.6 Gm. and thus represented only a small portion of the administered amino acid nitrogen. The chief portion appeared in the urine as urea. Phosphate was found practically to disappear from the urine as the parenteral regimen progressed. Since very little phosphate was given to the patients, its disappearance from the urine indicated a purposeful retention. Serum phosphate levels were usually in the low normal range. Sulfate was excreted at nearly constant rates, the nitrogen-sulfur ratios ranging from 1:14 to 1:20, which is of the same order as in normal feeding. Creatinine excretion was remarkably variable and for the most part lower than normal. All these observations are to be the subjects of further investigations.

In clinical practice, it is not necessary to adhere to the use of amino acids as the exclusive source of protein, as was done in this investigation for the purpose of nitrogen balance studies. Much more satisfactory responses can be expected if parenterally injected amino acids are supplemented with dietary protein whenever the patients are capable of taking food by mouth. Furthermore, in view of the anemia of these patients, massive injections of whole blood are indicated. Transfusions of 2,000 cc. have been found by us to be superior to injections of plasma or amino acids for producing an immediate elevation of serum protein concentrations. Thus the combined use of protein, blood transfusions, carbohydrate intake of 300 Gm. or more and paren-

21. Lusk, G.: *The Physiological Effect of Undernutrition*, Physiol. Rev. 1:523, 1921.

22. White, F. R., and Belkin, M.: *Sources of Tumor Proteins: I. Effect of a Low-Nitrogen Diet on the Establishment and Growth of a Transplanted Tumor*, Nat. Cancer Inst. 5:261, 1945.

23. Whipple, G. H., and Madden, S. C.: *Hemoglobin, Plasma Protein and Cell Protein—Their Interchange and Construction in Emergencies*, Medicine 23:215, 1944.

the fracture has solidly healed. The metal bar can then be removed and used again.

Clement<sup>130</sup> reports a study of 32 cases of march fracture in which the fracture was oblique in all early cases and the second and third metatarsal bones only were involved; these were longer than the first metatarsal bones in all but 2 cases, and the fracture line appeared on the medial surface in 29 cases. The increased length of the second and third metatarsal bones deranges the normal tripod structure of the foot, and march fracture results from stress and strain as a result of leverage on the bones, muscle pull of the lumbricalis and interosseus dorsalis muscles, which become spastic from irritation induced by marching.

Bosshardt<sup>131</sup> states that the high incidence of march fracture in German and Swiss armies is due to rigid cadence of marching. There is a definite difference between the occurrence in these two armies and that in the French army, which has an easy marching rhythm. American soldiers generally have led sedentary lives and have poor muscle tone and are therefore liable to have march fracture. The author believes that the fracture is primary and is related to a preexisting static disturbance of the foot, on which rhythmically repeated subthreshold mechanical insults have been acting. The treatment consists in rest and in physical therapy which incorporates exercises especially for dorsal and plantar flexion at the metatarsophalangeal joints.

Salmon's<sup>132</sup> report is based on 5 cases of march fracture. He relates that the absence of a history of direct trauma is responsible for some missed diagnoses. The characteristic appearances of the bone changes in the roentgenograms are described. Immobilization and rest are the suggested therapeutic measures.

Hullinger and Tyler<sup>133</sup> report 313 cases of march fracture in recruits undergoing training. The series includes a small number of cases of stress fractures in bones other than the metatarsals. It is believed that in 100 additional cases there were early march fractures which were completed by a definite trauma, but these cases have not been included in the series. A

detailed statistical analysis is made of the possible relationship of age, weight and other factors to the causation of the condition. The most interesting conclusion is that there is no predisposition to march fracture by any anatomic defect or variation, either acquired or congenital. The roentgenograms in the present series have been compared with three hundred roentgenograms of feet chosen at random. Measurements were taken of metatarsal length, width and spacing; position and conformity of sesamoid bones; length and width of feet, and general formation of foot. "There was no essential difference in the average of measurements in the two groups."

The general conclusion is that march fractures are brought about by trauma in the form of repeated subthreshold insults to the bone caused by walking. The determining factor is essentially a physiologic weakness secondary to fatigue. The incidence of march fractures is directly related to the severity of the training program. A new training order increasing the load carried by a man and the amount of exercise taken immediately resulted in a sharp increase in the number of patients with march fractures admitted to the hospital. The authors favor treatment by immobilization in a light walking plaster cast. They believe that if the bone is not protected from strain in this way callus will be excessive and recovery delayed. With treatment as outlined, all but 2 of the subjects returned to the full rigorous training program in an average of thirty-three days from the time of diagnosis.

[ED. NOTE.—The incidence of march fracture has increased because of the war so that it dominates the literature on the foot. The various reports seem to be in accord with regard to the history, symptoms and findings. There is some variation with regard to causation, but most authors feel that the change in the bone is a matter of strain and that there is an imbalance between the capacity of the bony structure and the demand made on these structures. The result is a disturbance which leads to the hypertrophic changes and the actual fracture. The treatment varies somewhat, although the consensus seems to be that more protection is needed, particularly in the acute phase. The rehabilitation of the foot to gain maximum capacity, so that the patient can carry out the duties of a soldier as soon as possible, is also stressed. This can be accomplished by means of walking casts or by means of a new device, a longitudinal steel bar in the shoe. This seems to fulfil the prerequisites of protection of the metatarsal bone and early resumption of activity.]

130. Clement, B. L.: March Fracture: A Common Disability of the Foot, *J. Bone & Joint Surg.* **26**:148-150 (Jan.) 1944.

131. Bosshardt, C. E.: March Fracture: A Common Disability of the Foot in Military Practice, *Arch. Phys. Therapy* **25**:41-44 (Jan.) 1944.

132. Salmon, J. K.: March Fracture, *J. Roy. Nav. M. Serv.* **30**:1-5 (Jan.) 1944.

133. Hullinger, C. W., and Tyler, W. L.: March Fracture: Report of Three Hundred and Thirteen Cases *Bull. U. S. Army M. Dept.*, September 1944, no. 80, pp. 72-80.

pared by E. A. Bering Jr.<sup>15</sup> made spongy porous and called fibrin foam. In use it soaked in thrombin, squeezed out and laid the bleeding surface. The texture of the material presented a meshwork in which clot could form, and the sponginess aided by drawing blood into the meshes.

This material was studied on monkeys and 95 patients. It was found to have a speedy and reliable hemostatic effect and to be absorbed by the tissues with but minimal reaction. The substance was made available to the armed forces, and a recent report by Woodhall<sup>16</sup> recounts its satisfactory use in 226 operations in rehabilitation neurosurgery.

2. *Oxidized Cellulose*.—The conversion of cellulose (surgical cotton or gauze) to an organic acid by the action of nitrogen dioxide renders that material soluble at the alkalinity present in tissue juices and absorbable by the body.<sup>17</sup> It was employed by Putnam<sup>18</sup> as a carrier for thrombin, but the recent disclosure of Seegers and Doub<sup>19</sup> that thrombin is inactivated by the acidity of oxidized cellulose (about  $pH$  4) invalidates his results. The acidity can be neutralized with 1 per cent sodium bicarbonate and the material is then harmless to the clotting agent.<sup>20</sup> In general, however, oxidized

cellulose should be classed as an absorbable pack rather than as a thrombin carrier, and it possesses, perhaps fortunately, a slight stypticity helpful in prevention of ooze.

3. *Starch Sponge*.<sup>21</sup>—This substance is non-irritating and readily absorbable, but the samples so far available have been found friable and impractical for use in surgical practice.

4. *Gelatin Sponge*.—The recent announcement by Correll and Wise<sup>22</sup> of the successful production of an absorbable, spongelike matrix derived from gelatin relieves the precarious dependency on human blood as the source of the foam type of thrombin carrier. Gelatin, like fibrin foam, is a protein but with the important distinction of being a nonspecific, "universal" protein devoid of antigenicity and therefore procurable from any animal. Beef is the common source. Because gelatin is a soluble substance, the problem was to convert it from a soluble to an insoluble but absorbable material. By suc-

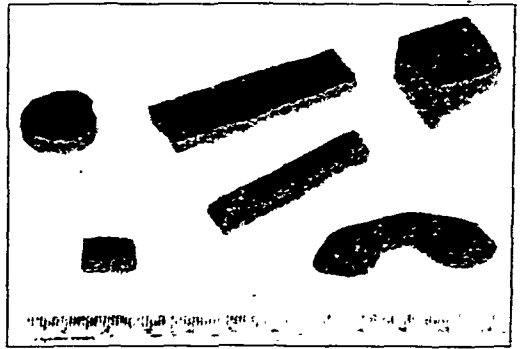


Fig. 1.—Specimens of gelatin sponge.

F. D.; Bailey, O. T., and Nulsen, F. E.: Studies on Fibrin Foam as a Hemostatic Agent in Neurosurgery, with Special Reference to Its Comparison with Muscle, *ibid.* 1:171-181, 1944. Bailey, O. T., and Ingraham, F. D.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XXI. The Use of Fibrin Foam as a Hemostatic Agent in Neurosurgery; Clinical and Pathological Studies, *J. Clin. Investigation* 23:591-596, 1944. Ingraham, F. D., and Bailey, O. T.: Clinical Use of Products of Human Plasma Fractionation: III. The Use of Products of Fibrinogen and Thrombin in Surgery, *J. A. M. A.* 126:680-685 (Nov. 11) 1944.

15. Bering, E. A., Jr.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XX. The Development of Fibrin Foam as a Hemostatic Agent and for Use in Conjunction with Human Thrombin, *J. Clin. Investigation* 23:586-590, 1944.

16. Woodhall, B.: Fibrin Foam as a Hemostatic Agent in Rehabilitation Neurosurgery, *J. A. M. A.* 126:469-471 (Oct. 21) 1944.

17. Yackel, E. C., and Kenyon, W. O.: The Oxidation of Cellulose by Nitrogen Dioxide, *J. Am. Chem. Soc.* 64:121-127, 1942. Unruh, C. C., and Kenyon, W. O.: Investigation of the Properties of Cellulose Oxidized by Nitrogen Dioxide, *ibid.* 64:127-131, 1942.

18. Putnam, T. J.: The Use of Thrombin on Soluble Cellulose in Neurosurgery: Clinical Application, *Ann. Surg.* 118:127-129, 1943.

19. Seegers, W. H., and Doub, L.: Oxidized Cellulose and Thrombin, *Proc. Soc. Exper. Biol. & Med.* 56:72-73, 1944.

ceeding at the same time in foaming it into an efficient sponge, which can be wetted, wrung out and refilled indefinitely, the special physical properties which gave success to fibrin foam as a thrombin carrier have been duplicated. Gelatin sponge is, in fact, more efficient. A cubic centimeter weighs only 9 mg., yet it will absorb nearly 0.5 Gm. (forty-five times its weight) of water or blood (fig. 2). It is free from the friability of fibrin foam, can be cut with a scalpel without disintegration and is obtainable from the

20. Uihlein, A.; Clagett, O. T., and Osterberg, A. E.: The Use of Oxidized Cellulose for Hemostasis in Surgical Procedures: Preliminary Report, *Proc. Staff Meet., Mayo Clin.* 20:29-32, 1945. Seegers and Doub.<sup>19</sup>

21. Bice, C. W.; MacMasters, M. M., and Hilbert, G. E.: Proposed Use of Starch Sponges as Internal Surgical Dressings Absorbable by Body, *Science* 100:227-228, 1944.

22. Correll, J. T., and Wise, E. C.: Certain Properties of a New Physiologically Absorbable Sponge, *Proc. Soc. Exper. Biol. & Med.* 58:233-235, 1945.

In a report of 200 cases of foot disorders selected at random from the orthopedic clinic, Burnham<sup>141</sup> concluded that it would be better carefully to eliminate men with severe foot disorders at the induction centers because it is difficult under military conditions to treat these disorders so that the men can perform useful service. He believes that an improved orthopedic shoe should be issued to all soldiers who exhibit some foot weakness and that the shoe should protect the trainee against acute foot strain which leads to a pes planus. He also urges conservative measures rather than any radical operation with regard to the treatment in military service.

Hauser<sup>142</sup> states that the cause of most common foot disorders is functional decompensation or an imbalance between the work required of the foot and the capacity of the foot to do the work. Increase in load may cause this; standing on hard surfaces and wearing stiff-shanked shoes or shoes with high, narrow heels are causative factors. If the foot is in valgus position, it should be brought into varus position. Shoe corrections may help; a medical wedge on the heel and a comma-shaped bar higher on the outside, which does not go under the fifth metatarsal bone, to bring the anterior part of the foot into relative pronation, is recommended. In addition, the patient must be taught how to stand and how to walk and given special foot exercises. He must have rest periods which are controlled and functional exercises graded to individual needs.

Cleveland, Willien and Doran<sup>143</sup> have operated on 25 soldiers, including 1 officer and a nurse. In 22 of the cases the patients' subsequent fate is known. Half of the soldiers operated on for a single bunion returned to full duty, but only 13 per cent of those with bilateral bunions returned to full duty after operation. A comparison of different operative procedures led the authors to believe that Keller's operation is the method of choice because of good and quick healing, relatively simple after-treatment and a quicker recovery than after other operations. It is emphasized that in general the results of operations for hallux valgus in soldiers are unsatisfactory and that no operation for bunion should be undertaken, especially for bilateral bunions,

unless there seems to be a reasonable prospect of the soldier's return to full duty.

Silver and Rusbridge<sup>144</sup> state that in view of the relative frequency of sprains of the ankle a method of treatment which returns the soldier to active duty in the shortest time with minimum of disability or hospitalization is greatly to be desired. At a station hospital in North Africa, 74 patients with severely sprained ankles were treated in nine months. Of these, 67 returned to active duty immediately and 2 had associated chip fractures of the lateral malleolus (1 returned to duty immediately and the other was overnight in the hospital because of no transportation). The cases of the 6 remaining patients, who were hospitalized, are analyzed.

The authors advocate a basket weave ankle strapping that does not encircle the leg at any point and that is applied with the foot at right angles to the leg and in neutral position regarding varus and valgus. Strapping the foot in inversion is condemned. Compound tincture of benzoin is applied to the skin prior to the strapping. Immediate use is recommended. They attempted to treat 5 patients with injections of procaine hydrochloride into the tender areas, without strapping. All obtained complete relief at once and walked out unassisted, but all returned the next day limping and with recurrence of disability and pain. They were then treated with a basket weave type of strapping, with good results.

Snow and Kraus<sup>145</sup> describe a method of administering procaine hydrochloride by iontophoresis for painful limitation of motion. The technic consists in the application of a solution of 1 per cent procaine hydrochloride and a 1:20,000 solution of epinephrine in 80 per cent alcohol. A gauze pad two to four layers thick is soaked in the solution and placed over the area to be treated. A crash towel is folded twice, soaked in isotonic solution of sodium chloride and spread over the gauze. A flexible metal electrode which is smaller than the towel is then placed over it. The positive pole of a source of galvanic current is attached to the metal electrode. The electrode is fixed by means of bandages. A neutral electrode of approximately the same size is moistened with weak saline solution and connected to the negative pole. The current is slowly applied and increased to 20 milliamperes and permitted to flow for twenty minutes.

144. Silver, C. M., and Rusbridge, H. W.: The Treatment of Sprains of the Ankle. *M. Bull. North African Theat. Op.* (no. 5) 1:26-28 (May) 1944.

145. Snow, W. B., and Kraus, H.: Novocaine Iontophoresis for Painful Limitation of Motion. *Mil. Surgeon* 95:360-362 (Nov.) 1944.

141. Burnham, W. H.: Army Foot Disabilities, *Mil. Surgeon* 95:20-24 (July) 1944.

142. Hauser, E. D. W.: Common Foot Disorders: Rehabilitation with Physiologic Exercises, *Arch. Phys. Therapy* 25:93-95 (Feb.) 1944.

143. Cleveland, M.; Willien, L. J., and Doran, P. C.: Surgical Treatment for Hallux Valgus in Troops in Training at Fort Jackson During the Year of 1942, *J. Bone & Joint Surg.* 26:531-534 (July) 1944.

cluded operations for brain tumor, subtemporal decompression, elevation of depressed skull fracture, scalenotomy, ligation of the carotid artery and laminectomy. The material was found exceptionally efficient and reliable in controlling the types of bleeding for which the patch technic is suitable, and it afforded easier handling, wider

contributions they have rendered to the new technic.

**Method of Using Gelatin Sponge:** The control of bleeding by the use of gelatin sponge soaked with thrombin may be compared to repairing a tire by the use of a rubber patch and a vulcanizing substance. Gelatin sponge is the



Fig. 4.—*A*, gelatin sponge twenty days after implantation on injured brain, showing lymphocytic and giant cell reaction and breaking up of material. *B*, gelatin sponge thirty days after being embedded in brain. Material is disappearing, and there is lymphocytic and giant cell reaction.

latitude of application and fewer failures than did fibrin foam. Fundamentally, however, fibrin foam and gelatin sponge serve the same purposes, and the extensive experiences with fibrin foam reported by Ingraham and Bailey and by Woodhall should be consulted for the important

patch and thrombin the vulcanizer. Whereas, however, the tire patch itself is impervious, the gelatin has been foamed—for a special reason—into a porous sponge and becomes an impervious seal only after blood flows into the meshes, mixes with thrombin and clots.

foot in full dorsiflexion. A cast was worn two weeks, and roentgen ray check-up showed a normal left ankle. On this day the cast was removed and weight bearing allowed. In four days the swelling was no longer present, and good motion of the joint was present without pain or stiffness. The patient was discharged on full duty in approximately four weeks after the injury.

Braun<sup>149</sup> expresses great satisfaction in the results he obtained by conservative therapy for bilateral acquired pes cavus deformities of severe degree in a 24 year old seaman. The treatment consisted in manual stretching of the contractures, restoration of the articular function by manipulation, fulcral felt blockings and strapings, physical therapy and an appliance to establish proper balance of the feet with weight bearing. He states that this case demonstrates what success can be obtained by an intelligent approach to this condition.

Boyd<sup>150</sup> reports 4 additional cases of talonavicular synostosis, the patients being a white girl of 10 years, a white boy of 10 years, the boy's father aged 45 and the boy's grandmother aged 72. The relationships of the last 3 patients suggest a hereditary nature of the condition.

Cohen<sup>151</sup> reports an additional case (20 previous cases have been reported in the literature) of osteochondritis dissecans of the astragalus. An operation two weeks after the trauma afforded an opportunity to note capsular damage (ecchymosis) which may account for this lesion. Necrosis was rapid and probably occurred immediately after the vascular damage or, at most, within several weeks. A description of the observations at operation for the removal of the osteochondritic body, the microscopic pathologic changes and the differential diagnostic points between an osteochondritic body and a post-traumatic osteochondral fracture are presented.

Croce and Carpenter<sup>152</sup> state that tearing of the plantaris tendon or tennis leg occurs most frequently in middle-aged persons. The syndrome does not cause much disability and has not been widely investigated. The immediate cause of this syndrome and the end result are not definitely known. The authors present a case history which is unusual for three reasons: 1. The cause was direct trauma. 2. The tear

occurred near the origin of the muscle belly. 3. The injury resulted in a degenerative tumor of the muscle. It would seem that the plantaris tendon was torn from its origin along the linea aspera and probably deprived of its blood supply and a degenerative reaction of the belly of the muscle resulted.

Bickel and Moe<sup>153</sup> have described an operative procedure for the relief of paralytic calcaneal deformity of the foot resulting from poliomyelitis in 13 patients. The method consists in translocating the peroneus longus tendon by sliding it intact around the lateral border of the heel into a groove in the midline of the os calcis in an attempt to improve on the results obtained when the peroneal tendon is cut and transplanted into the tendo Achillis. They concluded that the best results were obtained when the operation was done on patients who had slight remaining power in the gastrocnemius muscles and fair or better power in the transposed peroneal muscle. It was their opinion that the results were strikingly better than if the peroneal tendon had been cut and then transplanted into the tendo Achillis.

A case of hereditary malformations of the hands and feet has been traced through four generations by Stiles and Pickard.<sup>154</sup> The defects in the extremities ranged from gross splitting of the hand or the foot to slight abnormalities of the digitis. An inspection of the pedigree reveals that the trait may be inherited as a single dominant. Modifying genes, environmental factors or a combination of both may be responsible for the extreme polymorphism of the character.

Experimental fractures in rabbits were treated by Blum<sup>155</sup> with phosphatase and calcium glycerophosphate with and without an anchoring medium (an alginate gel) employed to prevent the too rapid diffusion of the introduced enzyme from the region of the bone gap. Enzyme and substrate were either injected into the gel, which had been pressed into the bone gap, or were injected into the bone gap, in which the gel was subsequently formed *in situ*. Progress of repair of the bone was followed by roentgenograms and by histologic examination. The treated fractures showed acceleration of repair as compared with untreated controls.

149. Braun, G. S.: Bilateral Pes Cavus: A Case Report, U. S. Nav. M. Bull. 43:346-348 (Aug.) 1944.

150. Boyd, B. H.: Congenital Talonavicular Synostosis, J. Bone & Joint Surg. 26:682-686 (Oct.) 1944.

151. Cohen, H. H.: Osteochondritis Dissecans of the Astragalus, Bull. Hosp. Joint Dis. 4:86-91 (Oct.) 1943.

152. Croce, E. J., and Carpenter, G. K.: Rupture of the Plantaris Muscle, J. Bone & Joint Surg. 26:S18-S20 (Oct.) 1944.

153. Bickel, W. H., and Moe, J. H.: Translocation of the Peroneus Longus Tendon for Paralytic Calcaneus Deformity of the Foot, Surg., Gynec. & Obst. 78:627-630 (June) 1944.

154. Stiles, K. A., and Pickard, I. S.: Hereditary Malformations of the Hands and Feet, J. Hered. 34:341-344 (Nov.) 1943.

155. Blum, G.: Phosphatase and the Repair of Fractures, Lancet 2:75-78 (July 15) 1944.

w Staphylococcus albus. Other bacteria, including Staphylococcus aureus and Escherichia coli, and a nonpathogenic fungus were present occasionally in small numbers.

The number of organisms obtained from the wound just before closure was considerably greater than the numbers recovered in the first two cultures. This is probably due to the fact

TABLE 1.—Results of Culture in Cases of Inguinal Herniorrhaphy

Operation	Culture of Skin Before Incision, Number and Type of Colonies	Culture of Wound After Incision in Skin, Number and Type of Colonies	Culture of Wound Before Closure, Number and Type of Colonies	Culture of Skin After Operation, Number and Type of Colonies
1	Left: no growth Right: 1 fungus; 14 Staph. albus	1 Staph. albus No growth	1 B. subtilis 9 Staph. albus	164 Staph. albus 206 Staph. albus; 1 fungus
2	No growth	No growth	2 Staph. aureus; 1 Staph. albus	70 Staph. albus
3	2 Staph. albus	2 B. subtilis; 1 Staph. citreus	1 B. subtilis	Uncountable Staph. albus
4	Right: 2 Staph. albus Left: 43 Staph. albus; 2 Staph. aureus	56 Staph. albus 4 Staph. albus	100 Staph. albus 21 Staph. albus	Uncountable Staph. albus and citreus Uncountable Staph. albus and citreus
5	2 E. coli	No growth	12 Staph. albus; 2 E. coli	Uncountable Staph. albus
6	Right: no growth Left: no growth	2 Staph. albus 3 Staph. albus	56 Staph. albus 400 Staph. albus; 50 sarcina	Uncountable Staph. aureus and albus Uncountable Staph. aureus and albus
7	Right: 1 Staph. albus Left: 1 fungus	No growth No growth	No growth 400 Staph. albus and citreus	Uncountable Staph. albus and citreus; 100 E. coli Uncountable Staph. albus and alpha; streptococci
8	No growth	20 Staph. albus	8 Staph. aureus; 105 Staph. albus	Uncountable Staph. albus and E. coli
9	No growth	No growth	No growth	4 Staph. albus; 1 fungus
10	1 sarcina	2 Staph. albus; 1 fungus	25 Staph. albus	Uncountable Staph. albus

TABLE 2.—Results of Culture in Miscellaneous Operations

Operation	Culture of Skin Before Incision, Number and Type of Colonies	Culture of Wound After Incision in Skin, Number and Type of Colonies	Culture of Wound Before Closure, Number and Type of Colonies	Culture of Skin After Operation, Number and Type of Colonies
1. Cholecystectomy and appendectomy	2 Staph. albus	No growth	Uncountable E. coli	20 Staph. albus; 5 E. coli
2. Radical mastectomy	25 Staph. albus; 6 Staph. aureus	No culture	11 Staph. albus; 1 fungus	120 Staph. albus
3. Colectomy	1 Staph. aureus	1 Staph. citreus	32 Staph. albus and citreus	10 Staph. albus
4. Posterior gastroenterostomy	Uncountable B. subtilis; 1 Staph. albus	5 B. subtilis	1 Staph. albus	Uncountable B. subtilis; 1 Staph. albus
5. Radical mastectomy	2 Staph. albus	No culture	12 Staph. albus; 1 fungus	31 Staph. albus; 2 fungi
6. First stage thoracoplasty	No growth	No growth	No growth	1 Staph. albus; 1 fungus
7. Repair of ventral hernia	32 Staph. aureus and albus	48 Staph. albus and citreus	12 Staph. albus	75 Staph. albus
8. Subtotal thyroidectomy	3 fungi	No growth	1 Staph. albus; 2 fungi	80 Staph. albus; 2 fungi
9. Exploratory laparotomy	No growth	2 Staph. albus	12 Staph. albus	82 Staph. albus
10. Radical mastectomy	No growth	No culture	1 Staph. albus	128 Staph. albus

In the second culture, it is shown that in most instances a few organisms are carried into the wound with the skin knife. They are of the same variety as those obtained from the surface of the skin, are relatively nonpathogenic and belong to the resident flora.

that the bacteria which gained entrance to the wound multiplied during the time of operation. Some of them possibly gained entrance to the wound in perspiration flowing over the skin edges, regardless of the fact that towels were closely applied. These bacteria also belong to the resident flora and are relatively nonpathogenic.

## PANCREATITIS

### AN ANATOMIC STUDY OF THE PANCREATIC AND EXTRAHEPATIC BILIARY SYSTEMS

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In the majority of diseases of the upper part of the abdomen, the symptoms are sufficiently well defined to permit a definite diagnosis. Probably the most prominent exception in this respect is the pancreas. At the same time, this organ is often involved in pathologic conditions of the surrounding viscera and even in diseases of more remote regions. The problem of pancreatitis is the old problem of abdominal surgery and, since a direct attack on the pancreas is as yet fraught with so much danger, a proper consideration of prepancreatic and peripancreatic disease, together with the etiologic factors as forerunners of acute and of chronic pancreatitis, becomes of vital importance. There is ample evidence<sup>1</sup> to prove that cholecystitis and acute and chronic pancreatitis coexist in a large percentage of cases, but the cause of such coexistence is still obscure.

Where does the provocative agent come from? Among the many explanations of the cause of pancreatitis, the one attributing the condition to a reflux of bile into the pancreatic duct seemed the most plausible to the greatest number of clinicians until Rich and Duff,<sup>2</sup> seeking the cause of acute hemorrhagic pancreatitis in cases in which there was no ampulla of Vater, conclusively demonstrated that in some cases acute hemorrhagic pancreatitis is due to metaplasia of the epithelium of the duct with associated dilatation of the duct and acinar rupture behind the

obstructing metaplasia. And yet a cursory review of the literature on acute pancreatitis is sufficient to impress on one that there is still a striking lack of agreement among investigators concerning the cause. In order to understand the problem, it is necessary to assemble all the information available and then to weigh the interrelations of these facts.

#### HISTORICAL ASPECTS

The earlier anatomists, among them Galen and Vesalius, gave little thought to the pancreas, believing that it acted as a cushion to support and protect the stomach and adjacent structures; and it was not until 1641 that Moritz Hoffmann first discovered the duct of the pancreas while working on a rooster and showed his findings to Wirsung, who one year later dissected the duct in the pancreas of a human body, thus making possible a proper interpretation of its physiology. In a letter to Jean Riolan Jr., professor of anatomy in Paris, Wirsung gave the world the first account of his important discovery. Wirsung had a drainage of the duct reproduced on a copper plate,<sup>3</sup> from which but few copies were struck off. According to Choulant,<sup>4</sup> only two copies are known to be preserved. Schirmer<sup>5</sup> saw one in the University of Strasbourg and had a photolithographic reproduction of it made.

To G. Dominici Santorini<sup>6</sup> belongs the credit for the first description of the accessory pancreatic duct and for the first representation ap-

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1. Edgahl, A.: A Review of One Hundred and Five Reported Cases of Acute Hemorrhagic Pancreatitis, with Special Reference to Etiology, with a Report of Two Cases, *Bull. Johns Hopkins Hosp.* 18:130, 1907. Mayo, W. J.: *The Surgical Treatment of Pancreatitis*, Surg., Gynec. & Obst. 7:607, 1908.

2. Rich, A. R., and Duff, G. L.: Experimental and Pathological Studies on the Pathogenesis of Acute Hemorrhagic Pancreatitis, *Bull. Johns Hopkins Hosp.* 58:137, 1936.

3. Wirsung, G.: *Figura ductus cujusdam cum multiplicibus suis ramulis noviter in pancreate observ*, Padoue, 1642.

4. Choulant, J. B.: *Geschichte und Bibliographie der anatomische Abbildungen*, Leipzig, R. Weigel, 1852.

5. Schirmer, A. M.: *Beitrag zur Geschichte und Anatomie des Pankreas*, Inaug. Dissert., Basel, L. Reinhardt, 1893.

6. Santorini, G. D.: *Anatomici summi septemdecim tabulae*, Parmae, ex regia typog., 1775, p. 150, tabulae XII and XIII.



not feasible surgically or has not been complete for one reason or another recurrence has been the rule. Furthermore, in patients with multiple lesions the surgical attack on one of the lesions in association with the use of penicillin will result in the healing of the lesion subjected to operation, while the other lesions remain uninfluenced until such time as they are in turn subjected to operative therapy in conjunction with the administration of the drug.

The necessity for the surgical eradication of the osteomyelitic lesion creates of itself the difficult problem of healing the resultant rigid-walled cavity. The only exceptions are those instances in which amputations are performed. Healing can be accomplished by one of two methods. The usual method resorted to in recent times depends on the filling of the rigid-walled cavity with granulation tissue from the depth and periphery of the wound to its surface and the subsequent epithelization of the débrided area. The success of this method depends largely on the speed with which these granulations fill the wound. Unfortunately, the growth of granulation tissue proceeds satisfactorily to a certain point, subsequent to which growth becomes unequal in various parts of the wound and unduly prolonged. Healing finally comes to a standstill in many instances, resulting in the formation of sinuses and failure of closure of the wound. This is due to the gradual conversion of the aging granulation tissue at the periphery of the wound into fibrous tissue, resulting in the shutting off of the blood supply, as is characteristic of the formation of scar tissue. It therefore becomes evident that this method of healing of the saucerized area depends chiefly on the rapidity with which the granulation tissue proliferates to fill the cavity, for any undue delay results in the shutting off of the blood supply by the normal process of cicatrization.

The second method of healing of the saucerized area depends on various plastic procedures to obliterate or fill the rigid-walled cavity in association with primary or delayed closure of the wound. The use of foreign substances was formerly resorted to in an effort to obliterate the dead space. These procedures have usually failed because the antibacterial agents hitherto available were unable to control the element of infection of the hematoma, which perforce is present to a varying degree.

#### EXPERIMENTAL STUDIES

It is with these thoughts in mind—namely, the past history of the trials and the tribulations of the therapy of chronic osteomyelitis,<sup>4</sup> the patho-

logic status of the lesions and the problems encountered in the healing of this stubborn disease—that we have undertaken the project to study the usefulness of penicillin against this dread disease under a contract between the Office of Scientific Research and Development and the Hospital for Joint Diseases, on the recommendation of the Committee on Medical Research.

*Procedures.*—Each case was subjected to a painstaking review of the patient's history, physical observations and serial roentgenograms (when available), in order to evaluate the previous course of the disease. Bacteriologic examination included repeated cultures of the lesions and determinations of the susceptibility of the organisms to penicillin. Studies of the effect of the development of resistance to penicillin on the pathogenicity and physiologic processes of the organisms will be the subject of a separate report. Repeated determinations were made of the concentration of penicillin in the blood and urine of each patient by the method described by Rammelkamp.<sup>5</sup> In several instances the bone removed at operation was tested for the presence of penicillin. As a consequence of the observations cited in the introductory remarks, all but a few of the patients were subjected to an extensive saucerization operation.

*Dosage.*—With a few exceptions, all the patients received 20,000 units of penicillin intramuscularly every three hours. Infants and young children were given 10,000 units, as were also a few of the adults treated at the outset of this project. The duration of penicillin therapy depended on the clinical course of the patient. The total dose for each patient is recorded in tables 1 to 4.

In general, the size of the dose of penicillin administered was reflected in the concentration of penicillin in the patient's blood and urine. With a constant dose, the concentration of penicillin in successive samples of blood and urine from the same patient tended to be fairly constant. Raising or lowering the dose generally resulted in an increase or a reduction, respectively, of the blood level of the drug. However, variations

4. Buchman, J., and Blair, J. E.: *Maggots and Their Use in the Treatment of Chronic Osteomyelitis*, Surg., Gynec. & Obst. **55**:177-190 (Aug.) 1932. Buchman, J.: *Rationale of the Treatment of Chronic Osteomyelitis with Special Reference to Maggot Therapy*, Ann. Surg. **99**:251-259 (Feb.) 1934. Blair, J. E., and Hallman, F. A.: *Staphylococcal Antihemolysin-Titers Following Staphylococcal Toxoid in Chronic Osteomyelitis*, Proc. Soc. Exper. Biol. & Med. **34**:637-642 (June) 1936. Buchman, J.: *The Use of Staphylococcus Toxoid in the Treatment of Chronic Osteomyelitis*, J. A. M. A. **108**:1151-1156 (April 3) 1937; *The Rationale and Results of Maggot Therapy in Chronic Osteomyelitis*, New York State J. Med. **39**:1540-1553 (Aug. 15) 1939; *The Treatment of Chronic Osteomyelitis*, S. Clin. North America **122**:581-595 (April) 1942; *Osteomyelitis*, in Litchfield, H. R., and Dembo, L. H.: *Therapeutics of Infancy and Childhood*, Philadelphia, F. A. Davis Company, 1942, vol. 4, chap. 87, pp. 3732-3768.

5. Rammelkamp, C. H.: *A Method for Determining the Concentration of Penicillin in Body Fluids and Exudates*, Proc. Soc. Exper. Biol. & Med. **51**:95-97 (Oct.) 1942.

the body and the tail of the pancreas develop. Diverse views are still entertained concerning the duplicity of the ventral anlage, which arises in close proximity to the common duct. Some maintain that the bud is single, while others

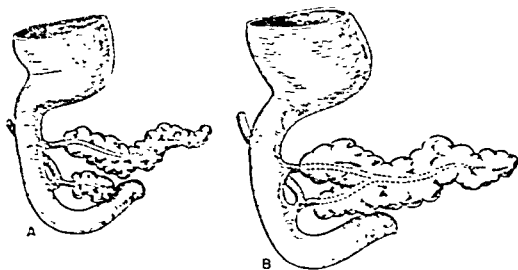


Fig. 1.—Pancreas of a human embryo: *A*, fifth week; *B*, seventh week.

rounded by pancreatic tissue; pancreatic tissue may occur even in the wall of the duct itself.

This relation of the exact point of origin of the persisting ventral bud to the common duct determines the final relation of the main pancreatic duct to the common duct. If the pancreatic anlage has grown out from the wall of the common duct itself, the final pancreatic duct will open into the ampulla of the common duct. If the pancreatic anlage has grown out from the wall of the common duct itself, the final pancreatic duct will open into the ampulla of the common duct. If the pancreatic anlage has grown out from the wall of the gut in close proximity to the common duct, the openings of the two ducts will be in close proximity, yet the

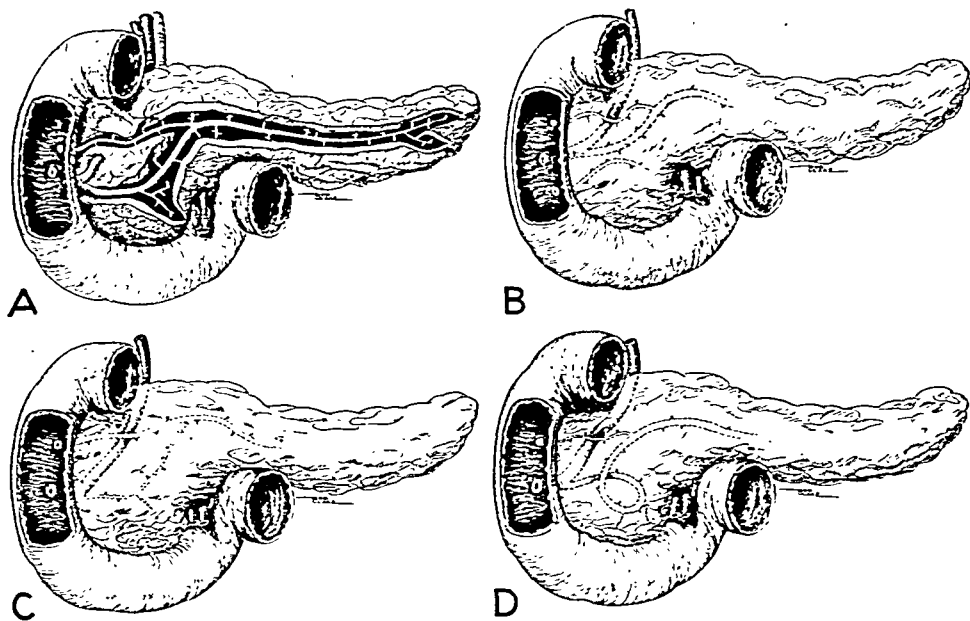


Fig. 2.—*A*, the most constant arrangement of the pancreatic ducts; *B*, specimen with three papillae; *C*, dissected specimen of an adult pancreas showing an embryonic type of duct system in which the accessory duct carries most of the pancreatic secretion; *D*, dissected specimen of an adult pancreas showing an unusual loop figuration of the main pancreatic duct.

old that at the beginning it consists of two lateral halves which subsequently fuse or one of which disappears, perhaps forming the source of aberrant pancreatic tissue often found along the wall of the gut. As development progresses, the ducts unite, as shown in figure 1 *B*, the duct of the dorsal anlage undergoing a certain degree of atrophy at its duodenal end<sup>11</sup> to produce the adult arrangement, shown in figure 2 *A*.

The close relationship between this portion of the pancreas and the common duct is thereby explained. Depending on the eccentricities of development, the relationship will vary somewhat: the common duct may be entirely sur-

rounded by pancreatic tissue; pancreatic tissue may really open into the intestine and not into the ampulla at all.

The facts seem to be these: Both buds develop by growth in continuity, the dorsal bud giving origin to all of the gland except that portion of the head in close proximity to the common duct and the intestinal wall. The persisting ventral bud grows out but a little way and then fuses with the dorsal bud, giving origin to but a small part of the glandular tissue of the caudal part of the head of the pancreas. In the majority of cases the duct system of this ventral anlage becomes the more important duct system from the point of fusion of the two anlages to the wall of the gut (fig. 1 *B*).

were only occasionally found, even though other secondary invaders occurred together with staphylococci in the majority of lesions. *B. pyocyaneus* and *B. proteus* were found in only 4 of 15 wounds, and in only 2 of these did they per-

TABLE 3.—*Lesions Treated by the Administration of Penicillin and Saucerization; Wounds Subjected to Delayed Closure*

Case and Lesion No., Age, Sex	Lesions			Penicillin				Cultures				Date of Operation	Comment
	Site	Duration, Yr.	Other Lesions	Dose, Thousand Units	Duration, Days	Local, Days	Total Amount, Thousand Units	Preoperative	At Operation	Postoperative	Increased Resistance		
3-4 28 M	Spine	10 mo.	Tibia	10	9	9	686	Sa Si	Sa Si	Sa Si	+	5/ 5/44	Large saucerized area healed in 31 days; see table 1, lesion 3-5 and table 2, lesion 3-6; healed at 10 months
12-19 39 M	Radius and elbow joint	7 mo.	Tuberculosis of same elbow	20	22	15	3361	Sa	Sa	Sa Si	0	7/15/44	Diagnosis of tuberculosis made on microscopic section; operative wound healed in 4 weeks; preoperative sinus left undisturbed and continued to discharge; see table 4, lesion 12-20
13-21 36 M	Hip	24	Ankylosed hip with intrapelvic soft tissue sinus into rectum	20	10	32	1506	..	Sa	Sa Si	+	9/ 5/44	Failure; sinuses persist; surgical eradication of lesion impossible
14-22 18 F	Tuberculosis of scapula with secondary staphylococcal infection	3	None	20	16	20	2471	Sa	.. Si	.. Si	..	8/15/44	Sinus outside of operative field persisted; operative wound healed per primam
15-24 16 F	Soft tissue sinus, thigh femur	2	None	20	9	28	1196	Sa Si	.. Si	.. Si	..	8/ 8/44	Wound contaminated with B. coli; healed in 43 days; healed at 5 months
16-25 10 F	Ilium	2½	None	20	15	13	1901	Sa	Sa	Sa	0	8/15/44	Sutures tied on third day; wound healed on 14th day postoperatively
17-26 22 M	Humerus	11 mo.	Tibia; carbuncle on back	20	19	22	3440	Sa	.. St	.. St	..	8/15/44	Wound and sinus healed in 16 days; carbuncles developed on back on 36th day postoperatively; humerus healed at 6 months
18-27 29 M	Tibia	25	None	20 10	16	16	1795	..	Sa	.. Si	..	8/22/44	Failure because of slough of skin; pinch graft 7 weeks postoperatively; healed 5 weeks later; penicillin ineffective; healed at 6 months
19-28 54 F	Hip	60	None	20 10	24	29	3121	Sa	Sa	.. Si	..	8/15/44	Sinuses were not excised or closed at operation; sinuses persist 9 months postoperatively
21-30 49 M	Spine, with multiple sinuses	14	Both tibias (inactive)	20	12	25	1581	..	.. St	Si	..	8/23/44	Transversectomy performed; complete eradication of focus and extensive sinus tract impossible; all wounds healed in 4 weeks; sinuses recurred 2 months after operation
23-31 22 M	Tibia	11	None	20 10	15	10	1646	Sa	.. St	.. Si	..	8/29/44	Healed in 5 weeks; part of skin sloughed; this healed in 8 weeks; healed at 7 months
23-32 39 M	Tarsus and metatarsal	23	None	20	10	17	1273	Sa	Sa	Sa	0	9/ 5/44	Wound broke down; believed to be because of inadequate surgical treatment; see table 2, lesion 23-33
24-34 12 F	Femur	1	Metacarpal	20	12	16	1530	Sa	.. St	Sa Si	0	9/ 5/44	Sinus outside operative field not closed at operation; discharge persisted; see table 4, lesion 24-35
28-44* 50 M	Spine	9 mo.	None	20	13	15	2018	Sa	Sa	Sa Si	..	9/23/44	Sinus persisted at 9 months
48-67 14 F	Tuberculosis of hip with secondary staphylococcal infection	4	None	20 10	16	26	2176	Sa	Sa	.. Si	..	8/22/44	Healed per primam, save at one point which was subsequently found to harbor a foreign body; see table 4, lesion 48-63

\* Patient treated by another member of the orthopedic staff and included through his courtesy.  
Sa — Staphylococcus aureus, coagulase positive.  
Sl — Secondary invaders.  
St — Sterile.  
+ — Staphylococci developed increased resistance to penicillin.  
o — Staphylococci did not develop increased resistance to penicillin.

ment parts; in like manner, a comparison relationship between the bile duct and the cystic duct reveals great variability. Furthermore, the method by which the bile duct and cystic ducts enter the duodenum is exceedingly variable, not only in closely related species but in individuals of the same species. Practically all textbooks of anatomy<sup>24</sup> describe these ducts as usually uniting to form a common duct at their duodenal extremities.

#### MATERIAL

The material in this study consisted of both fresh and adult human pancreases obtained from the autopsies in the department of pathology and fixed specimens from the department and also from specimens used in the dissecting courses in the department of anatomy at the Hopkins School of Medicine. The pancreases were from 150 men and 100 women ranging in age from 19 to 83 years. Death in no instance was caused by an atrophic process localized in either the duodenum or pancreas.

The entire work on the accessory pancreatic duct was carried out on 100 fresh autopsy specimens, because dissection of the duct after fixation was often difficult and at times the patency of the duct could not be accurately determined. The work on the main pancreatic duct and the common bile duct was carried out on 250 specimens, 100 of which were fresh and the remainder which were fixed, because of the difficulty encountered in preserving the delicate membranous septum which often separates the duct of Wirsung from the common bile duct.<sup>25</sup>

#### METHODS

The main pancreatic duct was first located by gross dissection in the middle of the neck of the gland, where the pancreatic tissue overlies the superior mesenteric vessels. Here the duct comes within 2 to 3 mm. of the surface and can readily be followed in either direction. The accessory duct was most quickly found by following the main pancreatic duct along its ventral surface toward the duodenum. In these anomalous instances in which the duct could not be found by this method or in which there was no apparent communication between the ducts, the second part of the duodenum was opened along its right free border and the position of the minor papilla was ascertained. Then, this being used as a guide, the accessory duct was sought for in the glandular tissue adjacent to the level of the papilla. In those instances in which no communication between the main and the accessory duct could be demonstrated even after pains-

taking dissection, the patency of the accessory duct and the minor papilla was established by inserting a small needle into the main duct and injecting air under minimal pressure while the entire specimen was submerged in water. If no bubbles emerged from the minor papilla, a hypodermic needle was inserted into the accessory duct to establish the patency of its duodenal end. Minimal pressure was used in order to avoid bursting of any natural barrier which might have been present at the blind duodenal end of the accessory duct.

If then no communication could be established, the main duct was injected with methylthionine chloride or eosin after the accessory duct had been ligated where the hypodermic needle had been inserted to test the patency of its duodenal end. Regurgitation of the dye evidenced the presence of a communication between the ducts.

The relation of the main pancreatic duct to the terminal part of the common duct was ascertained by incising the common duct near the entrance of the cystic duct and then opening it to its termination. Likewise, the pancreatic duct was followed from its communication with the accessory duct to its duodenal end, to ascertain what part, if any, it played in the formation of an ampulla. Careful measurements of the distance of the opening from the duodenal end of the bile duct were made with caliper points and recorded.

No attention was given to a study of the intestinal valves. The duodenum was opened along its right free border, and the major and minor papillae were identified in all specimens. Locating the major papilla presented no difficulty; the same, however, was not true of the minor papilla. Many times only after the most careful search could the minor papilla be found.

#### THE MAIN PANCREATIC DUCT

The main pancreatic duct begins in the tail of the gland through the convergence of several small duct radicles and pursues a more or less tortuous course through the body of the gland, approximating the dorsal and cephalic portions of the gland. In the head, however, the duct inclines caudally and dorsally, forming a wide arc with its convexity to the right, as it approaches the dorsal surface of the head of the gland. Reaching the level of the terminal part of the common duct, it runs horizontally to join with the caudal aspect of the common bile duct to form the major duodenal papilla.

In the 100 specimens studied for this purpose the tributaries of the main pancreatic duct in the body of the gland were observed to join the duct almost invariably at right angles and also to alternate with tributaries of the opposite side in the level at which they joined the duct (fig. 2A). The same arrangement was also present in the radicles of these tributaries, except in the head of the gland, in which this conformity was frequently departed from, both as to the position of the tributaries and as to their angle of junction. In 61 instances there was found a moderately large unpaired trunk, as shown in figure 2A, which drained the small lobe of

Gray, H.: *Anatomy of the Human Body*, edited by W. H. Lewis, ed. 22, Philadelphia, Lea & Febiger, p. 1191. Morris, H.: *Morris' Human Anatomy*, edited by C. M. Jackson, ed. 9, Philadelphia, P. Blakiston & Co., 1933, p. 1287. Cunningham, D. J.: *Cunningham's Textbook of Anatomy*, edited by A. H.enson, ed. 5, New York, William Wood & Company, p. 1194. Piersol, G. M.: *Human Anatomy*, edited by G. C. Huber, ed. 9, Philadelphia, J. B. Lippincott Company, 1930, p. 1737. Abeberry Oneto, A.: *Anatomía del duodeno y pancreas*, *Semana méd.* 27:395, 1920.

TABLE 4.—Lesions Treated by the Administration of Penicillin and Saucerization; Wounds Subjected to Primary Closure.—Continued

Case and Lesion No., Age, Sex	Lesions			Penicillin				Cultures				Date of Operation	Comment
	Site	Duration, Yr.	Other Lesions	Dose, Thousand Units	Duration, Days	Local, Days	Total Amount, Thousand Units	Preoperative	At Operation	Postoperative	Increased Resistance		
48-68 14 F	Tuberculosis of hip with secondary staphylococcal infection	4	None	20 10	19	At op.	1060	..	Si	Si	..	10/24/44	Healed per primam; walked for first time in 5 years; healed at 4½ months
49-60 14 M	Tibia	3½	None	20	17	At op.	2600	..	St	Sa	..	1/16/45	Healed per primam; small hematoma evacuated spontaneously; healed at 2½ months
7-75 36 F	Tibia	23	Multiple	20	17	At op.	2450	Si	Si	Si	..	1/23/45	Wound healed per primam, save for serosanguineous discharge from hematoma; completely healed on 42d day postoperatively; this lesion was saucerized and plastic surgical procedures performed on the skin permit primary closure; absorbable gauze left in situ; healed 2 months after operation; see table 1, lesion 7-12
50-73 26 M	Ilium	15	Carbuncles of axilla and leg	20 10	19	14	2750	..	St	Sa Si	0	1/ 2/45	Sinus persistent; soft tissue scar could not be excised completely; absorbable gauze left in situ; surgical treatment not adequate; amyloidosis; see table 2, lesion 50-70, and table 1, lesions 50-71 and 50-72
51-74 21 M	Ischium	3	Sinus to popliteal space	20 10	8	0	910	Sa	.. St	..	..	10/17/44	Tuberculosis of ischium with sequestrums and sinus leading to popliteal space; sinus secondarily infected with Staph. aureus; healed in 6 weeks; sinus persisted; operative site and sinus healed at 6 months
53-78 29 M	Femur	15	Right humerus and left forearm	20	20	1	3005	Sa	Sa	Sa Si	0	2/27/45	Failure, possibly due to inadequate operation; poor general condition; persistent hematoma
56-83 28 M	Femur	12	None	20	17	1	2638	Sa	Sa	.. St	..	3/ 6/45	Healed per primam; healed at 6 weeks
57-83 2 M	Humerus	2	Ulna	10	18	1	1300	..	St	*	..	3/ 9/45	Healed per primam; healed at 4 weeks
57-84 2 M	Ulna	2	Humerus	10	18	1	1300	..	Sa	*	..	3/ 9/45	Healed per primam; healed at 4 weeks
62-89 6½ mo. F	Rib	4½ mo.	None	10	12	..	870	.. Si	Sa Si	*	..	3/27/45	Rib resected; healed per primam; postoperative roentgenogram shows some residual disease
54-79 23 M	Femur	4	Humerus	20	14	1	2280	Sa	.. St	Sa	+	3/20/45	Healed per primam; 2 hematomas and stitch abscesses; lesion of humerus lighted up on 8th day of penicillin therapy and subsided in 7 days

Sa — Staphylococcus aureus, coagulase positive.

SI — Secondary invaders.

St — Sterile.

\* — No cultures after operation because wounds were healed. + Staphylococci developed increased resistance to penicillin.

0 — Staphylococci did not develop increased resistance to penicillin.

unit per cubic centimeters of saline infusion were obtained. In both instances coagulase-positive Staph. aureus was isolated from the operative wounds, and both strains had sensitivities of 0.06 unit. The method is only roughly qualitative at best. Since the penicillin content of subcutaneous tissues and body fluids approximates that of the blood serum,<sup>5</sup> it appears probable that relatively little penicillin can penetrate the avascular sclerosed bone surrounding an osteomyelitic lesion. If this is so, it is obvious that parenteral administration of penicillin without surgical intervention cannot be expected to provide therapeutic

cally adequate concentrations of penicillin at the site of bone lesions.

#### CONCLUSIONS

A clinical and bacteriologic study of the results of treatment of chronic osteomyelitis with penicillin with and without surgical intervention was made on 47 patients presenting a total of sixty-eight lesions. Some of the foci are listed in the accompanying tables more than once owing to the failure of one or another method of treatment. These are listed as separate lesions and are in-

Schieffer<sup>28</sup> on human fetuses and still later by Baldwin,<sup>29</sup> who made microscopic preparations of the terminal part of the accessory duct and the minor papilla.

The average diameter of the undistended duct in the 85 specimens with a normal duct arrangement at its point of perforation of the duodenal wall was 1.6 mm. The size of the duct, however, was no criterion of its patency, for only 62, about 73 per cent, were found to be patent by use of the injection method, whereby either air or dyes or both were injected under minimal pressure in order to avoid breaking through any natural barrier which might have been present. This gives, then, 23 specimens, about 27 per cent, which did not communicate with the duodenum. This is considerably higher than Helly's 20 per cent<sup>31</sup> and Baldwin's 10 per cent of 50 specimens,<sup>26</sup> in both groups of which the terminal part of the accessory duct was examined microscopically. These results, however, are in accord with those obtained by use of the injection technic (see table 2).

TABLE 2.—Patency of the Accessory Duct

	Injection Method	
	Patent	Closed
Schirmer.....	65	19
Charpy.....	9	21
Ople.....	79	21
Verneuil.....	20	0
Sappey.....	16	1
Rienhoff and Pickrell.....	62	23
Total.....	271	85
Per cent.....	76	24

In the 4 instances in which the duct system was reversed and the 11 instances in which no intraglandular communication of the ducts could be demonstrated, the accessory duct approached the duodenum with increasing caliber and with a patent papilla, leaving 23 per cent of all specimens in which the papilla was closed, regardless of the duct arrangement. Of practical interest, however, is the fact that in 11 per cent the ducts did not communicate and in 23 per cent the papilla was closed, making a total of 34 per cent in which fluid could not pass from the main duct to the duodenum by way of the accessory duct.

Complete absence of the accessory duct seems to be a rare anomaly, since it occurs in less than 1 per cent of specimens examined (table 3). Inversion of the ducts occurs in about 7 per cent (table 4).

28. Schieffer, J.: Du pancreas dans la série animale, Thesis, Montpellier, 1884.

#### RELATION OF THE AMPULLA OF VATER TO PANCREATITIS

Bécourt,<sup>29</sup> Bernard<sup>12</sup> and Laguesse<sup>30</sup> each mentioned 1 specimen in which the main pancreatic duct opened into the duodenum apart from the orifice of the bile duct. Schirmer<sup>5</sup> found 22 specimens, about 47 per cent, among 47 investigated in which a mucosal septum separated the orifice in such a manner that a true ampulla did not exist. Practically all textbooks of anatomy<sup>24</sup> describe the ducts as usually uniting to form a common channel at their duodenal extremities. Sappey<sup>25</sup> stated that this arrangement is the one which is observed in the great

TABLE 3.—The Accessory Duct

	Present	Absent
Schirmer.....	101	3
Charpy.....	29	1
Helly.....	50	0
Verneuil.....	20	0
Santorini.....	?	0
Bernard.....	?	0
Hamburger.....	50+	0
Sappey.....	17	0
Ople.....	100	0
Baldwin.....	76	0
Rienhoff and Pickrell.....	100	0
Total.....	543	4
Per cent.....		0.737

TABLE 4.—Inversion of Ducts

	Specimens Examined	Inversion of Ducts
Schirmer.....	104	4
Charpy.....	30	3
Bernard.....	?	1
Morel and Duval.....	?	1
Ople.....	100	11
Bimar.....	?	1
Moyse.....	?	1
Baldwin.....	76	3
Rienhoff and Pickrell.....	100	4
Total.....	410	29
Per cent.....		6.61

majority of cases. One of few exceptions to this view is found in the frequently cited work of Letulle and Nattan-Larrier,<sup>18a</sup> who found that a common channel occurred in only 8, about 38 per cent, of 21 specimens.

Schirmer<sup>5</sup> mentioned 11 specimens in his series of 47 in which the pancreatic duct opened into the bile duct and 14 specimens in the same series in which the bile duct opened into the pancreatic duct. Verneuil<sup>31</sup> seemed to believe

29. Bécourt, P. J. G.: Recherches sur le pancréas, Strasbourg, F. G. Levrault, 1830.

30. Laguesse, E.: Sur l'existence de nouveaux bourgeons pancréatiques accessoires tardifs, *Compt. rend. Soc. de biol.* 2:602, 1895.

31. Verneuil, A.: Mémoire sur quelques points de l'anatomie du pancréas, *Gaz. méd. de Paris* 6:384 and 398, 1851; reprint ed., Paris, E. Thunot & Cie, 1851.

anesthetized with pentobarbital,<sup>11</sup> renal extraction ratios for inulin and diodrast remain relatively constant and that for diodrast is so large (about 0.85) that plasma diodrast clearance is the near equivalent of renal plasma flow. However, during severe and prolonged hypotension the renal diodrast extraction ratio is depressed, so that diodrast clearance equals only a fraction (0.5 or even less) of renal plasma flow.

During and immediately after transfusion, diodrast clearance rises rapidly, often to levels exceeding normal. It might be concluded that the kidney responds to hypotensive ischemia by reactive hyperemia. Actually, renal blood flow is usually returned to, or is but little beyond, the normal level and soon falls. The temporary high diodrast clearance level when glomerular filtration is restored apparently results from the washing out of diodrast secreted into the tubules during hypotension. An example has been reported in a case of orthostatic hypotension.<sup>12</sup>

In summary, shock due to prolonged or repeated bleeding depresses renal function by causing a vasoconstrictive ischemia, which is not released by transfusion of blood and restoration to normal of arterial pressure.

The persistence of renal ischemia and anoxia in experimental shock due to bleeding seems to explain the prolonged renal functional depression which may follow bleeding in human beings. Therapeutically, it is significant that renal denervation does not prevent the vasoconstriction; hence there is no experimental basis for the treatment of posthemorrhagic urinary suppression by spinal anesthesia or paravertebral block. The nature of the abnormality makes the use of vasoconstrictor drugs illogical.

#### TOURNIQUET SHOCK

To mimic more closely the conditions of crush syndrome in human beings, renal function in dogs was studied during the onset of shock resulting from experimental application of tourniquets partially occluding arterial inflow. Details of the experiments have been reported elsewhere.<sup>13</sup>

11. Corcoran, A. C., and Page, I. H.: Effects of Anesthetic Dosage of Pentobarbital Sodium on Renal Function and Blood Pressure in Dogs. *Am. J. Physiol.* 140:234-239 (Nov.) 1943.

12. Corcoran, A. C.; Browning, J., and Page, I. H.: Renal Hemodynamics in Orthostatic Hypotension: Effects of Angiotonin and Head-Up Bed, *J. A. M. A.* 119:793-794 (July 4) 1942.

13. Corcoran, A. C.; Taylor, R. D., and Page, I. H.: Immediate Effects on Renal Function of the Onset of Shock Due to Partially Occluding Limb Tourniquets, *Am. Surg.* 11:671-676 (May) 1945.

The sequence of renal vascular changes (fig. 2) contrasts in some respects with that of the changes which follow bleeding. Arterial pressure is well maintained and even at first increased. In spite of this, renal blood flow decreases by about 20 per cent during the first fifteen minutes, by 50 per cent in thirty minutes and by 80 per cent in sixty to one hundred minutes after application of the tourniquet. Decreased renal blood flow without concomitant decrease in arterial pressure can result only from increased resistance to the flow of blood through the kidneys, brought about presumably by renal vasoconstriction. The glomerular filtration rate, measured as inulin clearance, is less decreased

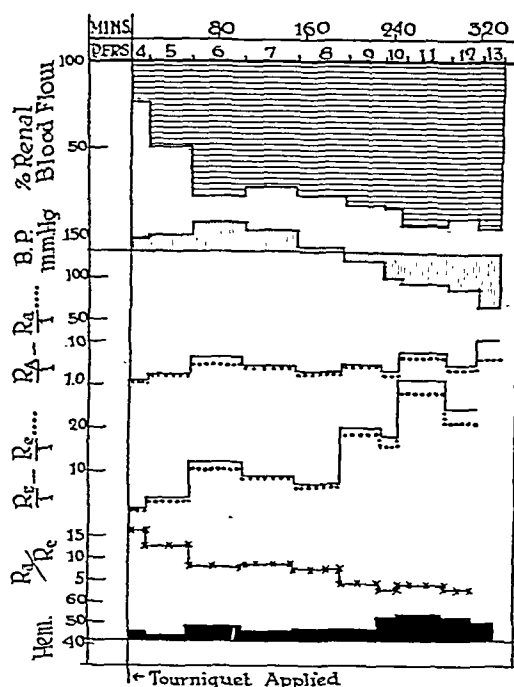


Fig. 2.—Percentage of normal total renal blood flow, blood pressure, hematocrit reading (*Hem.*), and concurrent changes in glomerular arteriolar afferent ( $R_A$  and  $R_A$ ) and efferent ( $R_E$  and  $R_E$ ) resistance during the onset of shock due to application of tourniquets to the limbs.

than is the rate of blood or plasma flow. The partial maintenance of glomerular filtration is due to an increase in intraglomerular pressure. Analysis of these changes according to formulas suggested by Lampport<sup>14</sup> indicates that the increase of intraglomerular pressure is due to predominance of constriction in the glomerular efferent arterioles, so that the function  $R_E$  (re-

14. Lampport, H. J.: Improvements in Calculation of Renal Resistance to Blood Flow: Charts for Osmotic Pressure and Viscosity of Blood, *J. Clin. Investigation* 22:461-470 (May) 1943.

at in 20 of 90, 22 per cent, specimens, the ampulla of Vater was absent and the ducts separated by a distinct septum. In 13 per cent, the distance from the orifice of the ampulla to the septum was 2 mm., and in 1 specimen the duct of Wirsung was reduced to a fibrous cord. No detailed measurements of the remaining specimens were given, except that the average distance from the apex of the ampulla to the septum was 4.8 mm.

Bélou, while making a special study of the biliary tract, investigated the relation of the duct of Wirsung to the common bile duct in 50 specimens and found that in 54 per cent the two opened into the duodenum, either separately or at the apex of the ampulla of Vater; in 30 per cent the duct of Wirsung opened from 1 to 2 mm. from the apex, while for the remaining 26 per cent measurements were lacking.

In Osler's series<sup>44</sup> of 100 specimens, in only 32 was the diverticulum of Vater of such size that a small calculus might occlude the orifice without completely filling it and obstructing one or both ducts entering it. Judd<sup>40</sup> studied 170 necropsy specimens for the purpose of determining the percentage of instances in which the anatomic arrangement was such that it would be possible to convert the two ducts into one continuous passageway. This was a possibility in only 4.5 per cent. He concluded that only very exceptionally is there an anatomic arrangement whereby the ducts can be converted either by a stone or by the action of a sphincter, into a continuous passageway permitting bile to flow from the common duct into the pancreatic duct.

Mann and Giordano<sup>41</sup> examined formaldehyde-fixed specimens obtained from 200 consecutive autopsies. Their technic consisted in simple dissection and measurement of the diameter of the ampulla and its duodenal orifice. In 90 specimens, 45 per cent, the ducts were contiguous and opened from 1 to 2 mm. from the apex of the papilla. In 28 specimens, 14 per cent, the length of the ampulla was 3 mm., while in only 7 specimens, 3.5 per cent, did it equal or exceed 5 mm. Since the average diameter of the ampulla was 2.5 to 3.5 mm. they reasoned that the common bile duct and the pancreatic duct could be converted into a continuous channel only by a blockage of the exit in the specimens in which the length of the ampulla was greater than the diameter of its duodenal orifice, i. e., in 7 instances, or 3.5 per cent. They called attention to the fact, previously noted, that the dimensions of the ampulla and the ducts entering it are

often such that a calculus which would become impacted would obstruct both ducts and would not convert them into a continuous channel.

Cameron and Noble<sup>42</sup> resorted to another method of investigation, which consisted in artificially impacting a carefully selected biliary calculus in the ampulla of Vater of a necropsy specimen by stripping it down the common duct and then determining whether a reflux occurred by forcing water or bile down the common duct under a pressure of 100 mm. or less and observing whether it escaped by way of the duct of Wirsung. To insure that the calculus was firmly lodged in the ampulla, a pressure of 1,800 mm. of water was brought to bear on the system. Irregular calculi were used most often, and not infrequently a part of the calculus protruded into the duodenum. Casts of these specimens in which a reflux occurred were obtained by pouring Wood's metal at 180 C. into the common duct, which ran up the duct of Wirsung and hardened immediately. When the cast was exposed, the points between which to measure were usually well defined.

After 100 specimens had been examined, an ampulla was found in 74 instances. In 8 of these, the size of the duodenal orifice was so great and the length of the ampulla so short that it was impossible to convert the two ducts into a common system by means of an impacted calculus. In the remaining 66, this was possible. They concluded, therefore, that in 66 per cent of 100 specimens it was anatomically possible for the common duct and the pancreatic duct to be converted into a single communicating system by an impacted biliary calculus. This figure contrasts sharply with Judd's 4.5 per cent in 170 specimens and Mann and Giordano's 3.5 per cent in 200 specimens.

#### STUDIES ON THE AMPULLA OF VATER

The foregoing review affords evidence that a considerable difference exists between the results of various observers. Because a more detailed study of the exact length of the ampulla of Vater is necessary, especially with reference to the percentage frequency of its variations, and in order to verify the reported discrepancies concerning the relation of the main pancreatic duct and the common bile duct, this study was undertaken.

The specimens consisted of 250 adult human pancreases obtained from both men and women ranging in age from 19 years to 83 years. Death in no instance was due to a pathologic process localized either in the pancreas or in the duodenum. Dissection was carried out in the fresh in 100 of the specimens, as previously outlined, and careful measurements were recorded with

44. Osler, W.: *Modern Medicine*, Philadelphia, Lea & Febiger, 1908, vol. 5, p. 637.



death rate of those myoglobin-treated animals with severe renal injury and great azotemia.

Structural changes in the kidneys of the metamycoglobin-treated rats were more severe in all categories of injury than in those given injections of isotonic solution of sodium chloride. Pigment casts and necrosis of all the distal

portion of vasoconstrictive ischemia, oliguria and aciduria, with the deposition in the kidneys of the muscle pigment, myoglobin. The state experimentally produced lends itself to the study of methods of clinical treatment.

*Treatment.*—Pertinent here is a brief selection of observations of immediate clinical significance. Some of the relevant data are presented in the table. From the point of view of treatment, the conditions of the experiments may be divided into those which (a) adversely and (b) favorably affect the outcome from the aspects of renal injury (azotemia) and mortality.

*Adverse Conditions.*—1. Dehydration by deprivation of water before crushing or by high environmental temperature (around 85 F.) results in increased renal injury and mortality. Gangrene of the injured limb is common when external temperatures are high and rare under conditions of moderate temperature. Parenteral administration of fluid as 0.9 per cent solution of sodium chloride to severely dehydrated animals after crushing and injection of metamycoglobin has little beneficial effect.

2. Injection of a large dose of a diuretic, such as 0.1 mg. of sodium sulfate per gram of body weight, increases immediate mortality, apparently by intensifying shock.

3. Intravenous injection of sodium citrate has been recommended in the early treatment of

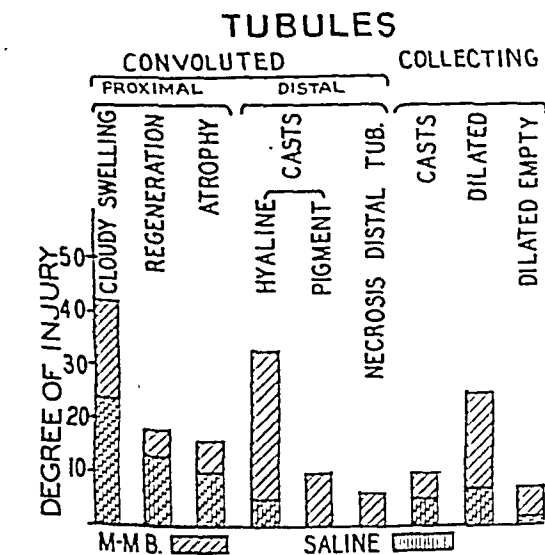


Fig. 6.—Summary of site and character of renal structural change in crushed rats treated with metamycoglobin (M-MB) and those given an equal volume of 0.9 per cent solution of sodium chloride. Structural changes were graded 1 to 4 plus, an arbitrary figure of 25 assigned to 1 plus, and the results averaged.

#### Effects of Treatment in Experimental Crush Syndrome\*

Group	Animals, Number	24 Hours		48 Hours		72 Hours	
		Blood Urea Nitrogen, Mg. per 100 Cc.	Death, Percentage	Blood Urea Nitrogen, Mg. per 100 Cc.	Death, Percentage	Blood Urea Nitrogen, Mg. per 100 Cc.	Death, Percentage
Sodium chloride control.....	47	63	6	52	5	51	2
Myoglobin control.....	96	90	25	89	15	64	4
Myoglobin-treated							
Sodium citrate.....	26	101	70	93	28	70	20
Sodium sulfathiazole.....	24	79	19	67	23	60	0
Diuresis, moderate.....	48	66	31	49	11	40	0
Gelatin.....	48	72	2	58	11	54	10
Gelatin lactate.....	24	65	6	43	10	33	11
Pressure bandage.....	22	79	0	52	0	56	0
Pressure bandage with diuresis.....	24	49	4	30	8	23	0
Pressure bandage with gelatin lactate..	23	35	9	23	9	19	0

\* Summary of mean levels of blood urea nitrogen and mortality per cent in control series given injections of isotonic solution of sodium chloride and myoglobin and in crushed rats given injections of myoglobin receiving various types of treatment.

tubules, such as appear in the crush syndrome in human beings, were present only in the myoglobin-treated animals.

Thus, from the aspects of azotemia, mortality and structural renal changes, the combination of crushing injury to skeletal muscles and injection of metamycoglobin into rats is shown to result in a state comparable to crush syndrome in human beings. Renal damage apparently is produced in human beings by a combi-

crush syndrome. Given in a dose of 0.1 mg. per gram of body weight, which is equivalent roughly to a dose of 5 Gm. for a human being, sodium citrate causes severe tetany, which is sometimes immediately fatal or which, by intensifying shock, greatly increases mortality during the first twenty-four hours. Survivors show no significant reduction in the degree of renal injury. The susceptibility to tetany of crushed animals treated with sodium citrate is ascribed to the

In the majority of instances, then, a calculus must be 4 mm. in diameter before it can cause obstruction, if one assumes that it is approximately spherical. This, however, seems the exception rather than the rule, since irregularly shaped calculi are encountered more frequently than spherical ones. This leaves, then, 47 specimens, about 18 per cent, in which the length of the ampulla exceeded the average diameter of the duodenal orifice and in which a complete block at the papilla by an impacted calculus would convert the ducts into a communicating system. This reasoning, however, is open to several serious objections. In the first place, conclusions formulated from measurements taken between poorly defined points, of differences of 1 mm. or less, seem decidedly inaccurate, since average measurements may never actually occur in a single instance. In the second place, the obstructing calculus was spherical, when irregularly shaped calculi are encountered more frequently, and, as suggested by Cameron and Noble,<sup>42</sup> a considerable part of an irregularly shaped calculus may project through the orifice of the ampulla into the duodenum, while its length may exceed that of the ampulla, and yet a reflux would be possible. It is true, also, that the greatest diameter of an impacted calculus may equal the long diameter of the ampulla in which it is wholly contained, with a communication existing between the ducts owing to the failure of the irregularly shaped calculus to completely fill the ampulla, which itself may be dilated.

Although it is a matter of definition as to whether an ampulla actually exists in those instances in which the septum extends within 2 mm. of the apex of the papilla, in table 6, in

TABLE 6.—*The Ampulla of Vater*

	Ducts Join to Form Ampulla	No Junction	Specimens Examined
Bécourt.....	?	1	?
Bernard.....	?	1	?
Laguesse.....	?	1	?
Schirmer.....	25	22	47
Letulle.....	8	13	21
Opie.....	22	11	100
Ruge.....	22	11	43
Baldwin.....	26	34	90
Belou.....	8	42	50
Mann and Giordano.....	40	160	200
Cameron and Noble.....	71	26	100
Rienhoff and Pickrell.....	51	160	250
Total.....	413	491	901
Per cent.....	46	53	

an ampulla is present in about 46 per cent, had the measurements been included in each investigator's report. For example, Cameron and Noble made no mention of the ampullae less than 5 mm., while in Opie's series of 100 specimens, in only 30 did this measurement equal or exceed 5 mm. Oser found only 32 of 100 specimens in which the diverticulum was of such size that a small calculus might occlude the orifice without completely filling it and thus obstruct both ducts. Our findings and the correlation of the greater part of the work done on this particular phase of the problem to the present time lead us to believe that the main pancreatic duct enters the duodenum apart from the common bile duct in 25 to 30 per cent of all cases and that a true ampulla is present in only 30 to 40 per cent.

#### THE RELATION OF THE SPHINCTER OF ODDI TO PANCREATITIS

Although Glisson<sup>45</sup> expressed the opinion that a sphincter existed at the end of the common bile duct, it was first described by Gage,<sup>46</sup> who studied the sphincter in the cat and found sphincters around the pancreatic and common bile ducts and one group of muscle fibers passing around both ducts. Oddi,<sup>47</sup> employing many species of animals, made an extensive comparative anatomic and physiologic study of the sphincter; but, aside from assigning a special sphincter to the duct of Wirsung, he did not study especially the relation of the sphincter of the common bile duct to the pancreatic duct. Somewhat later, Hendrickson<sup>48</sup> studied the sphincter in man, in the dog and in the rabbit. His specimens show muscle fibers surrounding both the common bile and the pancreatic duct.

In the absence of a stone in the ampulla of Vater, it has been suggested that in the instances in which both the bile and pancreatic duct open together in the ampulla, a flow of bile from the common duct might be diverted into the pancreatic duct during life by spasm of the sphincter of Oddi.

The possible importance of the sphincter at the duodenal end of the common bile duct was

45. Glisson, quoted by Oddi.<sup>47a</sup>

46. Gage, S. H.: The Ampulla of Vater and the Pancreatic Ducts in the Domestic Cat, *Am. Quart. Micr. J.* 1:123 and 169, 1878-1879 (pl. xii-xiv).

47. Oddi, R.: (a) D'une disposition à sphincter spéciale de l'ouverture du canal cholédoque, *Arch. ital. de biol.* 8:317, 1887; (b) Sulla tonicità dello sfintere del coledoco, *Arch. per le sc. med.* 12:333, 1888.

48. Hendrickson, W. F.: A Study of the Musculature of the Entire Extrahepatic Biliary System, *Bull. Johns Hopkins Hosp.* 9:221, 1898.

which the measurements are given a true ampulla was not considered present in the specimens. From the figures in table 6, we see that

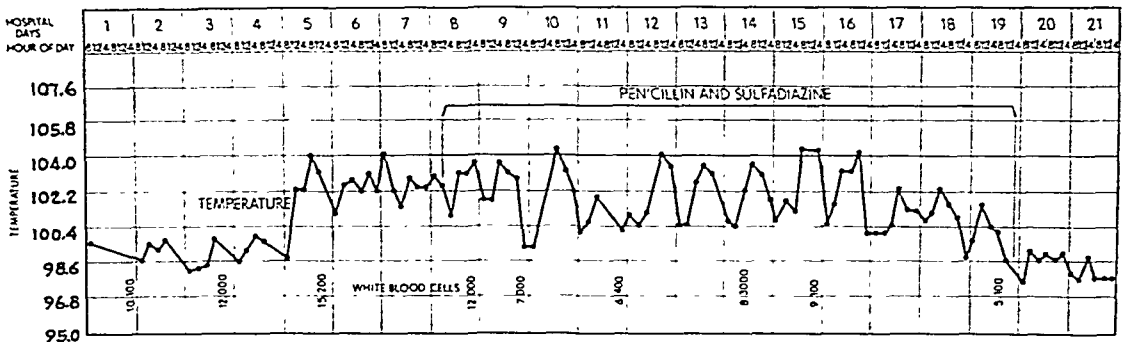
leukocytosis was present. The patient took food and fluids rather poorly by mouth, and hence from June 1 to June 8 she received 2,000 cc. of amigen with 5 per cent dextrose intravenously daily. From June 4 to 8 penicillin was given in a daily dose of 240,000 units; no sulfonamide drug was administered.

On May 23, 1944 Dr. William Adams made a 3 inch (7.6 cm.) incision 3 inches above the pelvis and extending to the umbilicus to drain the huge abscess filling the lower part of the abdomen. Green pus poured out under pressure. One Penrose drain was inserted and a dressing applied. Microscopic examination of two small hemorrhagic bits of tissue showed an extensive infiltration of inflammatory cells. The postoperative course was stormy, with a temperature ranging from 100 to 104 F. The diarrhea continued. The abscess drained freely. Anorexia persisted with occasional emesis. On June 22, 1944 a large abscess was found over the ninth, tenth and eleventh ribs on the right side. It was drained, 100 cc. of bloody, "tomato juice-like" purulent material being obtained. Culture disclosed *Streptococcus viridans* and *Esch. coli*.

The patient improved considerably. A roentgen ray examination of the colon on July 5 was reported as showing an old chronic ulcerative colitis involving the entire colon, with pronounced narrowing of the sigmoid flexure and with two fistulous tracts, one con-

inuation disclosed only a slight granularity and scarring of the rectal mucosa; it was not friable; no ulcers were seen. Roentgenograms of the gastrointestinal tract were normal. The stools were free from occult blood by the benzidine test; parasites were not found.

In September the patient went on a strenuous vacation, contracted a bad cold, became fatigued and also reached a critical point in the psychoanalysis she was undergoing. The diarrhea recurred and persisted, requiring hospitalization on October 20. The stools were watery, not bloody, eight or nine per day. The temperature varied between 98.6 and 99.7 F. The blood picture was normal. A proctoscopic examination showed the friable granular bleeding mucosa typical of chronic ulcerative colitis. On October 23 the patient was awakened at 2 a. m. with nausea and cramping abdominal pain. The only physical abnormality that could be detected was an area of tenderness about the umbilicus and in the epigastrium, just to the right of the midline. The temperature rose to 102 and 104 F. and remained high (see chart). The patient grew worse rather rapidly in the following days; the abdomen became distended and tender; the face was pinched; the appearance was that of acute toxemia; the white blood cell count was 15,200. Fluids were given by clysis. On October 26 the administration of sulfadiazine and penicillin was begun, 5.75 Gm. of



Temperature curve of case 2. The light line indicates the period of administration of penicillin and sulfadiazine.

necting with the cecum and the other probably with the hepatic flexure. The patient was discharged on July 20, 1944 and advised to return in two months for an ileostomy.

**CASE 2.**—A 35 year old white housewife dated the onset of her present disease back to 1933, when she had had an attack of "colitis" with innumerable liquid, bloody and mucous stools, a distressing "feeling of gas," painful cramps and discomfort in the abdomen. This syndrome recurred at intervals for a number of years. In 1941, when she was in Mexico, diarrhea developed again; the stools were examined on her return, and *Endamoeba histolytica* was found on two occasions. Treatment with emetine and vioform was followed by complete relief of symptoms. In May 1943 she experienced diarrhea, attributed to a food poisoning. After three weeks in a local hospital with no improvement, she entered Mayo Clinic in June, where Dr. Bergen confirmed the diagnosis of nonspecific ulcerative colitis. Repeated analyses of stools for *E. histolytica* were negative. Under treatment with azo-sulfamide, vaccine and a diet she improved remarkably.

In July 1944 she was referred to the University Clinics by her psychoanalyst for a routine examination. The bowel function was normal. The physical findings were essentially negative. Proctoscopic exam-

sulfadiazine in 500 cc. of isotonic solution of sodium chloride being given each day together with 100,000 units of penicillin by intramuscular injection, and increased on October 30 to 160,000 units. A transfusion of 500 cc. of whole blood was given on October 26 and 500 cc. of plasma the next day. A Miller-Abbott tube was passed, without relief of the abdominal distention. The pulse rate oscillated between 100 and 136 and the temperature between 101 and 104 F.; the abdomen was extremely distended. On November 4 the substitution of a Wangenstein tube for the obstructed Miller-Abbott tube resulted in the aspiration of a large amount of gas and fluid and greatly relieved the abdominal distention. This procedure was continued through the following days; the general aspect of the patient improved, and the temperature gradually dropped to normal. On November 6, because of the appearance of a rash, the use of penicillin and sulfadiazine was discontinued, a total dose of 1,580,000 units of penicillin and 41.25 Gm. of sulfadiazine having been given. Subsequent recovery was uneventful except for the annoying complication of a recurrent iridocyclitis.

**CASE 3.**—A 48 year old white grandmother came to the Albert Merritt Billings Hospital April 1, 1944, stating that for at least thirteen years she had had episodes of bloody diarrhea and abdominal cramps

was found. Duodenal lavage with magnesium sulfate was found to relax the sphincter, while hydrochloric acid caused temporary sphincter spasm, which can be prevented by atropinization. Morphine produces severe spasm lasting as long as four hours, with the pressure reaching 300 mm. of water during the second hour, after 16 mm. have been injected subcutaneously. The action of papaverine and epinephrine was found to be slight.

While there is disagreement as to the frequency with which bile can be held responsible for the development of acute hemorrhagic pancreatitis, all agree that if bile is injected under force into the pancreatic duct experimentally it can produce the condition, as was shown by Opie<sup>33</sup> and since then by many others. The experiments of Flexner<sup>57</sup> and those of other investigators demonstrate that the same result follows the injection of a wide variety of substances, such as oil (Oser,<sup>21</sup> Hess,<sup>58</sup> Guleke,<sup>59</sup> Eppinger<sup>60</sup> and Hewlett<sup>61</sup>), bile (Opie,<sup>33</sup> Flexner,<sup>57</sup> Guleke,<sup>59</sup> Oser<sup>21</sup> and Polya<sup>62</sup>), hydrochloric acid and intestinal secretion (Hlava,<sup>63</sup> Flexner and Pearce,<sup>57</sup> Hildebrand<sup>64</sup> and Rosenbach<sup>65</sup>), intestinal secretion and pancreatic juice, commercial trypsin, calcium and sodium chloride

(Polya<sup>62</sup>), sulfuric acid (Flexner and Pearce<sup>57</sup>), nitric acid (Flexner and Pearce<sup>57</sup>), zinc chloride (Lattes<sup>66</sup>), chromic acid (Lattes<sup>66</sup>), solution of formaldehyde (Flexner and Pearce<sup>57</sup>), calcium chloride (Binet and Brocq<sup>67</sup>) and oleic acid (Hess<sup>58</sup> and Trevor<sup>68</sup>). The same results have been obtained by injecting into the blood vessels substances such as oil, paraffin, wax and lycopodium (Panum,<sup>69</sup> Lépine,<sup>70</sup> Bunge<sup>71</sup> and Guleke<sup>59</sup>). Sailer and Speese<sup>72</sup> suggested that this great variety of substances that cause pancreatic necrosis on injection into the ducts is proof that mechanical distention and injury to the pancreatic tissue are the destructive agents. However, the following substances have been injected into the ducts without harmful effects: blood (Flexner and Pearce<sup>57</sup>) and (Guleke<sup>59</sup>), blood serum (Flexner and Pearce<sup>57</sup>), glycerin (Hess<sup>58</sup>), paraffin (Hess<sup>58</sup>), agar (Lattes<sup>66</sup>) and starch (Hess<sup>58</sup>).

While quantities of 4 to 30 cc. of bile and other fluids were injected forcibly into the pancreatic duct with a syringe, Rich and Duff<sup>2</sup> have shown that injections of smaller quantities of India ink into the pancreatic duct will rupture the smaller ducts and acini even in a large dog, leading to the immediate escape of ink into the interstitial tissues throughout the greater part of the pancreas. Archibald<sup>73</sup> was unable to produce necrosis or hemorrhagic pancreatitis by injecting small amounts (0.75 cc.) of bile into the pancreatic duct. Nordmann,<sup>74</sup> realizing the

57. Flexner, S.: The Constituent of the Bile Causing Pancreatitis and the Effect of the Colloids upon Its Action, *J. Exper. Med.* 8:167, 1906; Experimental Pancreatitis, *Bull. Johns Hopkins Hosp.* 9:743, 1900; On the Occurrence of the Fat-Splitting Ferment in Peritoneal Fat Necroses and the Histology of These Lesions, *J. Exper. Med.* 2:413, 1897. Flexner, S., and Pearce, R. M.: Experimental Pancreatitis, *Univ. Pennsylvania M. Bull.* 14:193, 1901.

58. Hess, O.: Experimenteller Beitrag zur Aetiologie der Pankreas- und Fettgewebsnekrose, München. med. Wchnschr. 50:1905, 1903; Experimentelles zur Pankreas und Fettgewebs-Nekrose, *ibid.* 52:544, 1905.

59. Guleke, N.: Demonstration einer experimentell gewonnenen Pankreasnekrose, *Berl. klin. Wchnschr.* 41:682, 1905; Ueber die experimentelle Pankreasnekrose und die Todesursache bei acuten Pankreaserkrankungen, *Arch. f. klin. Chir.* 75:845, 1905-1906; 85:615, 1908.

60. Eppinger, H.: Zur Pathogenese der Pankreasfettgewebsnekrose, *Ztschr. f. exper. Path. u. Therap.* 2:216, 1905-1906.

61. Hewlett, A. W.: On the Occurrence of Lipase in the Urine as a Result of Experimental Pancreas Disease, *J. M. Research* 11:1904.

62. Polya, E. H.: Zur Pathogenese der acuten Pankreasblutung und Pankreasnekrose, *Berl. klin. Wchnschr.* 43:1562, 1906; Ueber die Pathogenese der acuten Pankreaserkrankungen, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 24:1, 1912.

63. Hlava, J.: Some Affections of the Pancreas and Sudden Death from Them, *Sbírka přednášek z oboru lékařsk.*, v Praze, 1899, no. 16, p. 111; Sur la pancréatite hémorragique, *Compt. rend. Cong. internat. de méd.* (1897) (sect. 3) 2:106, 1899.

64. Hildebrand, G.: Zur Pankreaschirurgie, *Arch. f. klin. Chir.* 89:2, 1909.

65. Rosenbach, F.: Gallenstauung im Ductus Wirsungianus durch Stein in der Papilla Vateri als Ursache einer akuten Pankreasnekrose mit galliger Peritonitis, *München. med. Wchnschr.* 65:185, 1918.

66. Lattes, L.: Ueber Pankreasvergiftung, *Virchows Arch. f. path. Anat.* 211:1, 1913.

67. Binet, L., and Brocq, P.: Le rôle du suc intestinal dans la reproduction expérimentale de la pancréatite hémorragique avec stéatonecrose, *Compt. rend. Soc. de biol.* 83:340, 1920.

68. Trevor, R. S.: Some Recent Work on Disease of the Pancreas, *Practitioner* 72:570, 1904.

69. Panum, P. L.: Experimentelle Beiträge zur Lehre von der Embolie, *Virchows Arch. f. path. Anat.* 25:308, 1862.

70. Lépine, R.: Diabète maigre avec intégrité du pancréas, *Lyon méd.* 71:591, 1892.

71. Bunge: Zur Pathogenese und Therapie der acuten Pankreashämorrhagie und abdominalen Fettgewebsnekrose, *Arch. f. klin. Chir.* 71:726, 1903.

72. Sailer, J., and Speese, J.: Acute Pancreatitis, *Tr. A. Am. Physicians* 23:540, 1908.

73. Archibald, E. W., in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1933, vol. 7, p. 1.

74. Nordmann, O.: Experimente und klinische Betrachtungen über die Zusammengänge zwischen acuter Pankreatitis und Erkrankungen der Gallenblase, *Arch. f. klin. Chir.* 102:66, 1913.

those cases in which the patent ductus is uncomplicated by other serious developmental defects is ligation suitable. Bullock and colleagues<sup>1</sup> have stated the belief, however, that if infants under 3 years of age and patients with cyanosis are excluded the probability that patent ductus arteriosus is associated with other significant anomalies is relatively small.

Is the diagnosis of uncomplicated patent ductus arteriosus indication enough for operation? Shapiro<sup>2</sup> has suggested that, since the operative results are not uniformly good, only the patients demonstrating evidence of cardiac strain or stunting of growth should undergo operation until more accurate statistical data on the effects of surgical treatment are available. His own statistics, however, clearly show that patients with this disorder rarely live beyond the age of 40, usually succumbing to congestive failure or bacterial endarteritis as a direct result of the patent ductus arteriosus. His analysis<sup>4</sup> of 140 cases in which operations were performed reveals 72 per cent with completely successful results, with an over-all operative mortality of less than 10 per cent. Contrast these results with the extremely high mortality from the disease itself if untreated, and the answer is clear. Similar objections have been raised by Burch,<sup>5</sup> who stated that the surgical risk is still not good enough in average hands to recommend operation for all patients with patent ductus arteriosus. He lists as indications for operation subacute bacterial endarteritis, definite cardiac decompensation, especially if progressive, and mental and physical retardation. The development of these complications is, of course, indication for therapeutic ligation. But should one wait for complications to appear before advising ligation merely because the operative risk is not good enough in average hands? Should one cease recommending gastrectomy for patients with intractable ulcer because the mortality is prohibitive in average hands? It is true that the relative newness of the procedure precludes its evaluation on a basis of long term postoperative follow-up observations. One may assume, however, that the conclusions drawn from studies on the ligation of large vessels elsewhere in the body apply as well to the ductus arteriosus. If permanent obliteration of the lumen of the ductus is obtained, recanalization is unlikely to occur. Thus, if no other defect exists, this otherwise

irreversible condition can be reversed by surgical treatment and normal anatomic and physiologic relations restored. No long term follow-ups are necessary to attest this fact. From available evidence, therefore, prophylactic rather than therapeutic ligation appears to be the procedure of choice in competent hands.

#### OPERATIVE TECHNIC

All methods employed to date, short of complete division of the ductus, are attended by a certain number of recurrences. Gross<sup>2</sup> first employed simple ligation with silk. This method has been employed successfully in 2 of our cases (case 1 and 2). In 14 such cases, however, Gross had several failures due to the reopening of the channel. In his next 28 cases, following principles laid down by Pearse<sup>6</sup> for the gradual occlusion of large vessels, he wrapped the ligated duct with cellophane, in the hope that the fibrosis promoted by the cellophane would cause permanent obliteration of the lumen in 100 per cent of cases. Even this method was followed by some failures. The technic had definite advantages over simple ligation, however, as was demonstrated by Harper and Robinson<sup>7</sup> in their case of infected patent ductus arteriosus. They noted immediate disappearance of the murmur after double ligation of the duct followed by loose wrapping with cellophane. The murmur reappeared two weeks after ligation but had faded within two months, and by two and a half months it had again disappeared and remained permanently abolished. This late ablation of the murmur they attributed to occlusion by the fibrosis set up by the cellophane. Dr. John Alexander<sup>8</sup> has suggested that the fibrosis from the cellophane might be so intense that the large vessels in apposition to it might become stenosed or paralysis of the recurrent nerve might ensue. Neither complication has been noted in any of the cases in which cellophane has been used.

Because of the failure attending any method of occlusion of large vessels by ligation in continuity, Gross<sup>9</sup> began dividing the ductus. This, of course, increases the hazards of operation and demands not only a skilled operator and

6. Pearse, H. E.: Experimental Studies on the Gradual Occlusion of Large Arteries, *Ann. Surg.* **112**: 923-937 (Nov.) 1940.

7. Harper, F. R., and Robinson, M. E.: Occlusion of Infected Patent Ductus Arteriosus with Cellophane. *Am. J. Surg.* **64**:294-296 (May) 1944.

8. Alexander, J., cited by Harper and Robinson.<sup>7</sup>

9. Gross, R. E.: Complete Surgical Division of the Patent Ductus Arteriosus: A Report of Fourteen Successful Cases, *Surg., Gynec. & Obst.* **78**:36-43 (Jan.) 1944.

4. Shapiro, M. J., and Keys, A.: The Prognosis of Untreated Patent Ductus Arteriosus and the Results of Surgical Intervention, *Am. J. M. Sc.* **206**:174-183 (Aug.) 1943.

5. Burch, G. E.: Congenital Patent Ductus Arteriosus; An Evaluation of Its Surgical Treatment, *M. Clin. North America* **28**:388-402 (March) 1944.

the hemorrhage is the result of a vasomotor reflex; others believe that it results from venous thrombosis, and still others believe that it results from the erosion of the blood vessels by the pancreatic trypsin. Rich and Duff<sup>2</sup> found that the specific vascular lesion causing the hemorrhage was located especially in the media of the vessel, where the muscle fibers are swollen, their nuclei pyknotic and often separated by fluid spaces. The adventitia may appear condensed and pink staining and contain polymorphonuclear leukocytes. The internal elastic membrane becomes frayed, loses its undulations and takes on a swollen appearance. The first alterations of the media are found in its outer layers, the muscle fibers of which become necrotic while those near the intima remain intact. But the process is apparently a rapid one and proceeds rapidly to involve the entire thickness of the vessel wall, with final destruction of the intima. Destruction of a segment of the vessel wall was found most frequently in the larger arteries, while destruction of the whole circumference was the rule in the smaller vessels. The lesion is quite indistinguishable from that characteristic of the familiar arteriolonecrosis and hyaline arteriosclerosis occurring in man in association with hypertension and in arteriosclerotic nephritis.

#### SUMMARY

The historical aspects concerning the anatomy of the pancreas have been reiterated. The embryology of the pancreatic systems has been reviewed. The etiologic factors of pancreatitis have been discussed.

The anomalies and their results encountered in 250 dissections of the pancreatic systems are tabulated and discussed with their clinical significance. In 73 instances, about 24 per cent, there could be found no junction of the pancreatic and bile ducts, each entering the duodenum with

separate orifices. In 92 instances, 37 per cent, the ducts were contiguous, the dividing septum terminating 1 to 2 mm. from the apex of their common orifice. In this group, however, a true ampulla was not considered present. In 81 instances, 32 per cent, a true ampulla was present, varying in length from 3 to 14 mm., while in 4 instances, 2 per cent, the main pancreatic duct was reduced to a fibrous cord.

In 47 instances, 18 per cent, the length of the ampulla exceeded the average diameter of the duodenal orifice, and a complete block at the papilla would convert the two ducts into a communicating system.

The average diameter of the duodenal papilla was 3 mm., with limits of 1.5 and 4.5 mm.

Concerning the accessory pancreatic duct, in only 89 of 100 specimens studied for this purpose could any intraglandular communication between the ducts be demonstrated. In 4 instances, the embryonic duct system was present—i. e., the accessory duct carried the greater part of the secretion—while the main duct was reduced to a fibrous cord, leaving 85 specimens with a normal duct arrangement. In only 62 of these, 73 per cent, was the duct found to be patent, or there were 23 instances in which the accessory duct did not communicate with the duodenum, regardless of the duct arrangement, making a total of 34 per cent in which fluid could not pass from the main pancreatic duct to the duodenum by way of the accessory duct. The average diameter of the undistended duct at its point of perforation of the duodenum was 1.6 mm.

The anatomic position and arrangement of the sphincter of Oddi and the conditions modifying its resistance are discussed, and the current theories postulated regarding the necrosis and hemorrhage which occur are briefly discussed.

On May 18 the patient returned for a routine check-up. She had no complaints except occasional twinges of pain under the incision where the costal cartilages had been divided at operation. She had been feeling well and gaining weight. She no longer experienced dyspnea on climbing stairs and had had no orthopnea.

Examination revealed a well healed operative scar. No murmur was audible. Blood pressure in both arms was 110 systolic and 74 diastolic. Fluoroscopic examination and roentgenograms of the chest showed a decrease in size and pulsation of the pulmonary conus.

CASE 4.—N. H. D., a 20 year old white woman, was first admitted to the hospital on May 2, 1944, complaining of weakness, loss of weight and brown discoloration of the face of two months' duration. She gave no history of frank cardiac failure but admitted exertional dyspnea in excess of normal and occasional attacks of orthopnea. All her life she had been easily fatigued and had been unable to keep up with her playmates. She had also noticed some edema of the ankles. There was no history of chills or fever.

On examination the patient appeared well nourished and normally developed. There were splotchy brownish areas of discoloration over the face, neck and extremities. No thrill was present, but a loud machinery murmur with systolic accentuation was audible in the third left intercostal space. The heart was not enlarged. The blood pressure was 112 systolic and 60 diastolic. The remainder of the examination was essentially non-contributory.

The accessory clinical observations were: hemoglobin content 13.2 Gm. (85 per cent), erythrocyte count 4,050,000 and leukocyte count 6,160. The results of urinalysis were normal. Kahn, Kline and Mazzini tests of the blood elicited negative reactions. Electrocardiographic tracings were normal. Roentgenologic examination of the chest showed no evidence of cardiac enlargement, but the pulmonary conus was definitely prominent. Accentuation of the pulsations of the left ventricle, the aorta and the pulmonary vessels was noted.

A diagnosis of patent ductus arteriosus and chloasma was made. The patient and her family were advised of the dangers of a persistently patent ductus arteriosus, and ligation was advised. Operation was refused, and the patient left the hospital on May 17.

She returned on Feb. 20, 1945, stating that she wished to have the operation which had been advised nine months earlier, since her husband and her local physician had strongly urged her to have it.

The physical conditions were essentially unchanged. The murmur was still clearly audible, but no thrill was present. No additional observations were recorded.

The accessory clinical observations were identical with those of the previous admission.

On February 20, with the patient under endotracheally induced cyclopropane-ether anesthesia, the ductus was ligated, the technic described in case 3 being used. The duct in this case was smaller than that in the preceding case, measuring only 8 to 10 mm. in diameter and 12 to 15 mm. in length. The blood pressure changed suddenly at the time of ligation from 124 systolic and 74 diastolic to 124 systolic and 88 diastolic. The systolic pressure later fell to 110, but the diastolic pressure was maintained at 90.

Immediately after ligation the murmur disappeared and was not heard again during an uneventful convalescence. The temperature showed a slight rise to 101.1 F. on the second postoperative day but by the fourth day had returned to normal, where it remained without further variation. She received penicillin prophylactically for several days postoperatively. She was

out of bed on the eighth day and went home on the eleventh day. On discharge her blood pressure was recorded as 100 systolic and 70 diastolic; there was a decrease in pulse pressure of 22 mm.

The patient returned to the clinic for her regular postoperative examination six weeks after operation. At that time she had no complaints. She volunteered the information that she no longer noted the excessive fatigue and exertional dyspnea described before operation. She wanted to return to her old job in the mill. Examination revealed no thrills or murmurs. The blood pressure was 120 systolic and 60 diastolic.

CASE 5.—K. M. G., a 19 year old white married woman, was first treated at Duke Hospital March 4, 1939 for acute sinusitis. While in the hospital, a thrill and a to and fro machinery murmur were found in the second and third left interspaces. Albumin, red cells and casts were found in her urine. A diagnosis of a patent ductus arteriosus and chronic glomerulonephritis was made and conservative treatment initiated. The patient was readmitted twice during the following six weeks for her sinusitis, and an ethmoidectomy and a submucous resection were done. She was not seen again at this hospital until March 30, 1945, when she was examined in the gynecology clinic regarding sterility. The only abnormalities found were retroversion of the uterus and chronic cervicitis. Conservative treatment for these conditions was recommended. She was sent to the medical clinic for evaluation of her cardiac status. Because of the presence of a persistently patent ductus arteriosus, she was admitted to the surgical service on May 7 for consideration of ligation. A careful history was taken with regard to symptoms referable to her patent ductus arteriosus, and the following facts were elicited: She was unaware that there was anything wrong with her heart until approximately eleven years previously, when her local physician, during the course of a routine examination, found that she had a "leaking of her heart." Although she had never been able to keep up with other children because of excessive fatigability and dyspnea, she was not seriously bothered with the condition until several years prior to her present admission, when these symptoms became more pronounced.

Physical examination revealed a fairly well developed and nourished pale young white woman with a normal temperature, pulse rate and respiration rate. There was no cyanosis or clubbing of the extremities and no petechiae. The heart was not enlarged. There was a thrill over the second and third interspaces on the left with a systolic accentuation. A machinery murmur, also with systolic accentuation, was noticed over the same areas. A very soft apical systolic murmur was present. The blood pressure was 110 systolic and 70 diastolic in the left arm and 114 systolic and 70 diastolic in the right. The remainder of the physical examination was noncontributory.

Accessory clinical observations were: hemoglobin content 13.3 Gm. (86 per cent), erythrocyte count 4,590,000 and leukocyte count 9,080. Kahn, Kline and Mazzini tests of the blood elicited negative reactions. The blood nonprotein nitrogen level was 27 mg. per hundred cubic centimeters. Urinalysis showed nothing abnormal. A phenolsulfonphthalein test showed normal excretion of the dye. The electrocardiographic report was not indicative of myocardial disease. Fluoroscopic and roentgenographic examination of the chest revealed the lungs to be clear except for a moderate increase of vascular markings throughout both pulmonary fields. The pulmonary artery was prominent, with increased

ely, Stratman-Thomas and Eliot<sup>5</sup> and Knisely, Stratman-Thomas, Eliot and Bloch.<sup>6</sup>

4. The reactions of various parts of the vascular system during and following hemorrhage initiated with a minimum amount of mechanical trauma to animals (unpublished).

5. The reactions of the blood and vascular system and the changes in the circulation following mechanical trauma made with a minimum amount of hemorrhage from animals.

Thus, we have been studying normal blood and vessel walls, surveying the condition of these in a number of diseases and trying to study the sequence of circulatory phenomena seen in hemorrhagic shock uncomplicated by trauma, the sequence in traumatic shock uncomplicated by hemorrhage, and the pathologic circulatory phenomena in *P. knowlesi* malaria uncomplicated by either trauma or hemorrhage. The over-all purposes are, of course, to recognize as many factors as possible of normal and of pathologic circulatory physiology and to determine the kinds, magnitudes and sequences of pathologic factors present in each pathologic complex.

Our studies of the changes in blood and vessel walls preceding and during traumatic shock are a direct outgrowth of the microscopic studies of the pathologic circulatory physiology of rhesus monkeys during acute *P. knowlesi* malaria (see Knisely, Stratman-Thomas, Eliot and Bloch<sup>6</sup> and the motion picture "Knowlesi Malaria in Monkeys"). As outlined in the following paragraphs, the studies on malaria provided back-

ground for and clues to follow in this series of studies on traumatic shock.

#### METHODS

Two methods are being used for studying the blood and small vessels with microscopes. One is the fused quartz rod method of illuminating living tissues for microscopic study (Knisely<sup>8</sup> and Hoerr<sup>9</sup>), which permits routine study in many internal organs of experimental animals at 32, 48, 96, 240 and 400 and less frequently at 600 diameters' magnification. The other consists in focusing stereoscopic dissection microscopes (32, 48 and 96 diameters) on the obliquely illuminated nictitating membrane and/or bulbar conjunctiva of anesthetized animals or unanesthetized human beings. A Zeiss scale in one ocular permits rapid or continuous close estimates of the dimensions of structures observed.

At all times the blood coming down the arterioles of uninjured bulbar conjunctiva is a statistically valid sample of all the flowing arterial blood in the body. This was determined by opening an animal and studying the blood passing through many different organs. In frogs, observations under various approximately physiologic and known experimentally produced pathologic conditions have been made of the vessels and blood in skin, brain, peripheral nerves, smooth muscle of the gastrointestinal tract, gastric mucosa, mesenteries, striated muscles, lung, adrenal gland tissue, kidney and liver (for operative technics see Knisely, Bloch and Warner<sup>3</sup>). In mammals, observations have been carried out in the surface of brain, omentum, mesenteries, striated muscles, smooth muscles of the gastrointestinal tract, intestinal mucosa, uterus, ovary, spleen and liver. These studies have been carried out over a fourteen year period. At any one time, the blood coming down the arterioles of all organs of an animal has the same mechanical consistency. In about 3,500 frogs, in 1,100 salamanders (*Amblystoma*), in 500 small laboratory mammals—mice, rats, guinea pigs and cats (Knisely<sup>12</sup>)—and in 50 rhesus monkeys (Knisely, Stratman-Thomas, Eliot and Bloch<sup>6</sup>), this has always been true. Hence, the blood coming

5. Knisely, M. H.; Stratman-Thomas, W. K., and Eliot, T. S.: Observations on Circulating Blood in the Small Vessels of Internal Organs in Living *Macacus Rhesus* Infected with Malarial Parasites, *Anat. Rec. (supp.)* 79:90 (March) 1941.

6. Knisely, M. H.; Stratman-Thomas, W. K.; Eliot, T. S., and Bloch, E. H.: Knowlesi Malaria in Monkeys: I. Microscopic Pathological Circulatory Physiology of Rhesus Monkeys During Acute *Plasmodium Knowlesi* Malaria. *J. Nat. Malaria Soc.* 4: (Dec.) 1945.

7. At several points in this paper there are references to scenes in the motion picture "Knowlesi Malaria in Monkeys." This 16 mm. Kodachrome motion picture, taken through the microscope, records several scenes of normal unagglutinated blood and normal vessel walls and then traces one set of factors of pathologic circulatory physiology through lethal stages. The picture was made to make it possible to demonstrate some of our findings to physicians and medical scientists. It usually takes about sixty minutes to project the film. Copies of this film will be loaned free, except for transportation charges, to medical schools, medical societies, medical officers of the military services and research groups. Requests should be sent either to Dr. M. H. Knisely, Department of Anatomy, University of Chicago, or to Dr. T. S. Eliot, Department of Anatomy, University of Tennessee, Memphis, Tenn.

8. (a) Knisely;<sup>10</sup> (b) The Fused Quartz Rod Method of Illuminating Living Structures for Microscopic Study, in McClung, C. E.: *Handbook of Microscopical Techniques for Workers in Animal and Plant Tissues*, ed. 2, New York, Paul B. Hoeber, Inc., 1937, pp. 632-642; (c) An Improved Fused Quartz Rod Living Tissue Illuminator, *Anat. Rec.* 71:503 (Aug.) 1938.

9. Hoerr, N. L.: Illumination of Living Organs for Microscopic Study, in Glasser, O.: *Medical Physics*, Chicago, The Year Book Publishers, Inc., 1944, p. 625.



It is apparent from the studies of Lindau and Wulff,<sup>15</sup> Johnston and Renner<sup>16</sup> and Cobb<sup>17</sup> that the ulcers seen in Meckel's diverticulum are similar to gastrojejunal ulcers. About the only significant difference is the fact that the ulcers of Meckel's diverticulum occur primarily in childhood and gastrojejunal ulcers occur in middle age. This difference can be explained adequately on the basis that Meckel's diverticulum is a congenital anomaly whereas the gastrojejunal ulcer is the handiwork of the surgeon.

*Symptoms.*—Estes in 1932 described the predominant symptom as being pain one to one and a half hours after eating. This pain was similar to or more severe than the original ulcer pain and located to the left of the midline of the epigastrium, with tenderness at this point on palpation. Benedict described the symptoms of gastrojejunal ulcer as being pain, hematemesis and melena. He found that the pain was usually lower than the original pain and to the left of the umbilicus and sometimes extended to the left groin. Apparently this pain was not a predominant symptom after a fistula was established.

Walton reported that there were two definite groups of cases clinically. In the first, hematemesis is a predominant symptom, and in the second, and more common, variety, he found that in the earlier stages there were mild degrees of discomfort and flatulence. This was replaced later by definite pain simulating that from the original lesion, the attacks of pain being periodic but more severe than that from the original lesion and frequently awakening the patient at night. The pain, he found, was referred to the lower part of the abdomen and especially to the left iliac fossa. Vomiting was found to occur frequently and usually gave transient relief from the pain.

According to Wright, pain was the cardinal symptom in his series of 458 cases.

Walters and Clagett<sup>18</sup> in 1939 stated that a gnawing hunger type of pain came on between meals and occasionally awakened the patient at

night. The pain could be relieved by food or alkalis but was not as easily controlled as the distress of the original lesion. Although the pain could be epigastric, it frequently shifted below and to the left of the site of the original distress.

Rivers and Gardner<sup>19</sup> in 1940 concluded that the symptoms were similar to those produced by the original lesion but that gastrojejunal lesions were more penetrating, caused more constant distress and more distress at night and were less easily relieved by food and alkali. They mentioned that obstruction may distort the ulcer syndrome but that if there are no complications these lesions send pain along the splanchnic nerves as visceral phenomena. Pain of a perforating ulcer caused true stimulation of the spinal sensory nerves with referred pain along the distribution of the sensory nerves.

#### PRESENT INVESTIGATION

*Age.*—It was found in our study of 100 cases that gastrojejunal ulcer is a disease of middle age. The ages of the majority of patients (81) ranged from 30 to 59 years. The range of ages of the 100 patients was from 19 to 73 years. These figures compare favorably with the results of other investigations.

*Sex.*—Duodenal ulcer has been shown to be primarily a disease of men. Since most of the gastrojejunal ulcers in the cases herein studied followed operative procedures aimed to cure or relieve patients suffering from duodenal ulcers, it can be assumed that gastrojejunal ulcer should occur more often in men than in women. In the present study, 93 of the patients were men and 7 were women.

*Symptoms.*—Pain was the most common symptom of gastrojejunal ulcer in our patients. Pain of one sort or another was present in 86 per cent. Although pain was rather constantly encountered, its location varied greatly. In some the original pain produced by duodenal ulcer, which was usually in the epigastrium, occurred; in others the pain extended downward to either the right or the left side of the umbilicus or upward to the shoulder blades, as does the pain from cholecystic disease. At times the pain extended downward as far as the groin. This shifting of pain downward from its original site was described by 55 per cent of the 86 patients in whom pain was present and was not mentioned

15. Lindau, A., and Wulff, H.: Peptic Genesis of Gastric and Duodenal Ulcer, Especially in Light of Ulcers in Meckel's Diverticulum and Postoperative Ulcers in Jejunum, *Surg., Gynec. & Obst.* **53**:621-634 (Nov.) 1931.

16. Johnston, L. B., and Renner, G., Jr.: Peptic Ulcer of Meckel's Diverticulum: A Report of Two Cases and a Review of the Literature, *Surg., Gynec. & Obst.* **59**:198-209 (Aug.) 1934.

17. Cobb, D. B.: Meckel's Diverticulum with Peptic Ulcer, *Ann. Surg.* **103**:747-764 (May) 1936.

18. Walters, W., and Clagett, O. T.: Gastrojejunal Ulcer: A Study of One Hundred and Fifty-Five Cases, *Am. J. Surg.* **46**:83-93 (Oct.) 1939.

19. Rivers, A. B., and Gardner, J. W.: Recurrent Peptic Ulcer: Situation of Recurrences and the Importance of Studies of Pain in the Recognition of Such Recurrences, *J. A. M. A.* **115**:1779-1785 (Nov. 23) 1940.

once to a little more than twice or even two and a half times the diameter of the red cells which pass through them. The red cells usually pass in single file or, at most, a double row. When a capillary contracts or is compressed to just a little less than the diameter of the contained red cells, the red cells rub on the inner surface of the endothelium and thus resist passage, and the flow through that vessel soon stops (see Krogh,<sup>14</sup> page 11, and Knisely<sup>15</sup>). Most true capillaries can dilate without losing tonus, weakening and sacculating to a little more, but usually not much more, than two or two and a half times the diameter of the contained red cells (Krogh,<sup>14</sup> p. 335, and Knisely, Stratman-Thomas, Eliot and Bloch<sup>6</sup>). The arterioles of most of the organs in frogs and mammals which we have studied are long, narrow, tapering cones. During the flow of blood through them, their outlet tips vary either anatomically or functionally from a little wider to a little narrower than the capillaries or sinusoids they join and supply. These statements are true of the arterioles and capillaries of the bulbar conjunctiva of human beings and almost certainly true of the arterioles and capillaries of many other human organs during life. Arteriovenous anastomoses have thus far been found in but a few organs of any one species. The arteriovenous anastomoses which have been found are often closed and when open are frequently but two or three times the diameter of the red cells passing through them (see the reviews by E. R. Clark<sup>15</sup> and Boyd<sup>16</sup>). These are key points for understanding some of the pathologic processes initiated by intravascular agglutination of the blood, for they show that most of the time, under most conditions, nearly all the circulating blood must pass through vessels having an internal diameter from about once to twice or at most three times that of the red cells on every trip from the left side of the heart through the circulatory system and return. Thus, as is well known but not always remembered, the arterioles and capillaries are a perpetual "bottleneck" in the vascular system.

*C. Some Changes in the Blood and Vessel Walls During Stage III of P. knowlesi Malaria.*—At the beginning of stage III of the pathologic circulatory physiology of rhesus monkeys with *P. knowlesi* malaria, a thick, glassy precipitate forms between and around all the blood cells of the animal. In this malaria, this

precipitate forms throughout all of the animal's circulatory system at one time. The process acts as though it were autocatalytic; once it starts, it usually goes on to completion in from ten to about twenty minutes. This precipitate binds the animal's red cells together in wads and masses (*not rouleaux*), which by microscopic standards are large, semirigid and tough, and thereby rapidly changes all the animal's circulating blood into a thick, mucklike sludge.

As soon as the blood has changed to this thick, pasty sludge, a definite sequence of events takes place. Three major steps are as follows:

1. This sludge resists its own passage through small vessels much more than does normally fluid blood; consequently, the rate of flow through small vessels all over the body becomes progressively slower than the normal rates for each degree of dilatation of each vessel. This increased resistance to flow and consequent reduced rates of flow through the capillary beds slowly, progressively and inescapably leads to various degrees of stagnant anoxia all over the body.

2. There is a time interval of variable length during which (a) the reduced rates of flow are unmistakable and (b) there is still no visible hemoconcentration of the sludge passing through peripheral vascular beds. During this period, the flow through each small vessel is slower than the normal rate for whatever degree it is dilated but the vessels have not yet begun to leak perceptibly (see the scenes following titles 29, 30 and 31 in the Knowlesi Malaria film<sup>7</sup>). After the sludged blood has been flowing too slowly for a time, the walls of postcapillary venules and small venules lose their ability to retain blood colloids. Anoxia of the endothelium is alone sufficient to cause this (see Starr<sup>17</sup>; Starling<sup>18</sup>; Landis<sup>19</sup>; Krogh,<sup>14</sup> pp. 321, 326 and 335; Maurer<sup>20</sup>; Warren and Drinker<sup>21</sup>; Drinker,<sup>22</sup>

17. Starr, I., Jr.: Production of Albuminuria by Renal Vasoconstriction in Animals and Man. *J. Exper. Med.* **43**: 31 (Jan.) 1926.

18. Starling, E. H.: *Principles of Human Physiology*, ed. 4, Philadelphia, Lea & Febiger, 1926, p. 854.

19. Landis, E. M.: Micro-Injection Studies of Capillary Permeability: III. The Effect of Lack of Oxygen on the Permeability of the Capillary Wall to Fluid and to the Plasma Proteins, *Am. J. Physiol.* **83**: 528 (Jan.) 1928.

20. Maurer, F. W.: The Effects of Decreased Blood Oxygen and Increased Blood Carbon Dioxide on the Flow and Composition of Cervical and Cardiac Lymph. *Am. J. Physiol.* **131**: 331 (Dec.) 1940; The Effects of Carbon Monoxide Anoxemia on the Flow and Composition of Cervical Lymph, *ibid.* **133**: 170 (May) 1941; The Effects of Anoxemia Due to Carbon Monoxide

15. Clark, E. R.: Arterio-Venous Anastomoses, *Physiol. Rev.* **18**: 229 (April) 1938.

16. Boyd, J. D.: Arterio-Venous Anastomoses, *London Hosp. Gaz. (Clin. Supp.)* **42**: i (July) 1939.

vealed such a process (fig. 5 b). In view of these low figures, it is probably safe to assume that suture material does not play the significant role it was thought to play in the production of ulcer.

Magnesium silicate, such as is found in talc, also has been considered a foreign body capable of producing inflammatory changes and probably ulcers. The histologic preparations were examined under the polarizing microscope, and identification of the crystals was made according to the method described by Ramsey.<sup>20</sup> In approximately 8 per cent, magnesium silicate was found (fig. 5 c). Although this percentage is not large and certainly cannot be considered enough evidence for any conclusions concerning the role of magnesium silicate in the production of ulcer, the possibility that talc may be an etiologic factor should not be entirely overlooked. The obvious source of this foreign body is the talc (U. S. P.) used on surgeons' gloves.

The cases were reviewed in an attempt to correlate the severity of clinical symptoms with the pathologic changes, but little correlation was evident. In some instances of severe gastrojejunitis only mild symptoms occurred, whereas, on the other hand, in some cases of mild gastrojejunitis clinical symptoms were rather severe.

20. Ramsey, T. L.: Magnesium Silicate Granuloma, *Am. J. Clin. Path.* 12:553-558 (Nov.) 1942.

#### SUMMARY

The incidence of ulceration following gastroenterostomy for duodenal ulcer has been reported in the literature as varying from about 2 to 4 per cent. In general, the incidence reported in the literature for ulceration following gastroenterostomy for gastric ulcer is much less. In the present study, a detailed clinical and pathologic study was done in 100 cases in which resection of the stomach was carried out for gastrojejunal ulcer. Parietal cells were seen in the gastric mucosa adjacent to the gastric enteric stoma in the majority of these cases. In 81 of the 87 cases in which it was possible to determine the site of ulceration in relation to the anastomotic line, the ulcer occurred on the jejunal side, in 3 on the gastric side and in 3 on the anastomotic line. Simple epithelial cysts were found at or near the anastomotic line in approximately 1 in 5 cases. Brunner's glands were found occasionally in the jejunal mucosa adjacent to the stoma. The majority of cases showed gastrojejunitis of moderate or severe degree. There was little or no correlation between the degree of severity of the symptoms and the degree of gastrojejunitis. Suture material and magnesium silicate were found in the region of the gastroenteric stoma but appeared to have little direct relationship to the ulcer.

owly, but for a time the walls of vessels do not leak perceptibly. (3) When the flow has been slow enough for a long enough time, post-capillary venules begin to leak, at first slowly and then more rapidly. (4) Venule walls leak so rapidly that masses of coated cells are left stranded in the vessels. (5) The stranding of coated masses in vessels and loss of fluid from vessels causes a progressively decreasing circulating blood volume and venous return. (6) The rapid ingestion of coatings containing erythrocytes by the phagocytes of liver, bone marrow and spleen acts toward causing and maintaining (a) low red cell counts (anemia) and (b) progressively decreasing circulating blood volume.

*How Studies of Malaria Led to Studies of Traumatic Shock.*—When the formation of the stage III precipitate was seen with the microscope in a living monkey infected with P. knowlesi, the chemical and immunologic natures of the precipitate immediately became important problems. Consequently, samples of this heavily sludged stage III blood were drawn into oiled and heparinized or oiled and citrated syringes, injected into little petrolatum-ringed pools of citrated mammalian Ringer solution on microscope slides and examined by direct light and by dark field illumination.

In the living animal, all the red cells were held together in wads and masses. On the slide, not more than two minutes afterward, some clumps had separated; the rapid, forcible swirling of the blood as it passed into and out of the syringes and/or the solutions used caused many clumps to disintegrate into individual red cells. However, many masses of clumped red cells remained. By transillumination in vitro, the material which held these clumps together was not visible. By dark field illumination, it was obvious that a thick, glassy, cottony precipitate was present between and around all the red cells of each clump. (This is shown in the Knowlesi Malaria film following title 48 a).

Bloch pulled some of these clumps apart with a Chambers microdissector (see Chambers and Kopac,<sup>25</sup> pp. 62-109). The precipitate which held the erythrocytes together was fairly abundant and had a stringy or gluey or tarry consistency. By microscopic standards, it was rather tough. The appearance and consistency of the precipitate suggested that it might be largely

fibrin or some fibrin-like material. Consequently, we decided to try to form some fibrin within the vascular system of a normal monkey to see what freshly formed, intravascular fibrin would look like in the living animal.

#### MICROSCOPIC EXPERIMENTS WITH MECHANICAL TRAUMA

*1. Experimental Crushing of Monkey Omentum.*—A young, vigorous male monkey was selected and anesthetized with pentobarbital sodium given intrapleurally.<sup>26</sup>

When the animal was asleep, an eyelid was reflected (its tarsal plate keeps it flat) and the reflected portion transilluminated with a fused quartz rod to permit microscopic study of the circulating blood and the vessel walls of the inner surface of the eyelid. This area was then studied at 32, 48 and 96 diameters to see whether the blood and the vessel walls were normal. During these observations, made to help select a normal experimental animal and as controls for possible effects of the laparotomy which followed, the vessel walls and the blood flowing in them looked perfectly normal, for (a) the circulating red blood cells were not agglutinated, (b) each red cell which bumped a vessel bifurcation turned over easily, demonstrating that the plasma viscosity was within the normal range, (c) no white cells were sticking to the walls of small vessels, (d) no visible hemoconcentration was occurring in any small vessel, (e) there were no emboli in this area and no minute thromboses and (f) the flow of the normal unagglutinated blood in small venules was laminar, or "stream-

26. We did not want an anesthetic solution in high concentration on omental tissues which were to be observed with microscopes, and the rates of absorption from subcutaneous fascias are irregular and unpredictable. Solutions of crystalloids are absorbed rapidly from the pleural space, probably because (a) the outer surface of the lung has great numbers of capillaries, (b) the lateral pressure within lung capillaries is much less than that of the inwardly directed oncotic "attraction" force of the dissolved blood proteins, (c) the flow through these vessels is rapid and (d) there is a continuous mixing and spreading of films of fluid in the pleural space due to the respiratory excursions of the lung. Hence, the pentobarbital sodium was given intrapleurally.

The calculated dose of pentobarbital sodium is divided into fourths. At first, two quarter-doses are given: after fifteen minutes, the third quarter, and after fifteen minutes more, the fourth quarter-dose. A fifth quarter-dose is given later if necessary and an additional quarter-dose or eighth-dose given whenever necessary. This maintains a controlled, nearly even anesthesia. Care must be taken (a) to avoid the intercostal arteries and veins to prevent hemorrhage (a small needle [no. 27] is less apt to injure an artery than a large one), (b) to be sure to go all the way through the intercostal muscles and reach the intrapleural space and (c) to be sure not to injure the lung. As the lung has a wide respiratory excursion, it can be snagged on an inwardly projecting needle; the needle should not be pushed in any farther than necessary. We ground needle tips off a little to a smooth, rounded point, which can be pushed through the skin and muscle but is more apt to indent than to cut the resilient lung tissue.

25. Chambers, R., and Kopac, M. J.: *Micrurgical Technique for Study of Cellular Phenomena*, in McClung, C. E.: *Handbook of Microscopical Techniques for Workers in Animal and Plant Tissues*, ed. 2, New York, Paul B. Hoeber, Inc., 1937, pp. 62-109.

and rarefaction of the neck of the femur. This was definitely thought to be due to a pathologic fracture resulting from bony metastasis.

*Course.*—A biopsy of the femur at the fracture site was made on March 28. Microscopic sections showed interlacing bundles of spindle-shaped cells resembling smooth muscle cells and little intercellular substance.

mitotic figures were observed, and these were atypical forms.

The biopsy wound became infected, and there were an associated fever and leukocytosis. Culture of material from the wound grew beta hemolytic *Staphylococcus aureus*. Local irrigations and sulfamerazine by parenteral injection were given, without improvement.

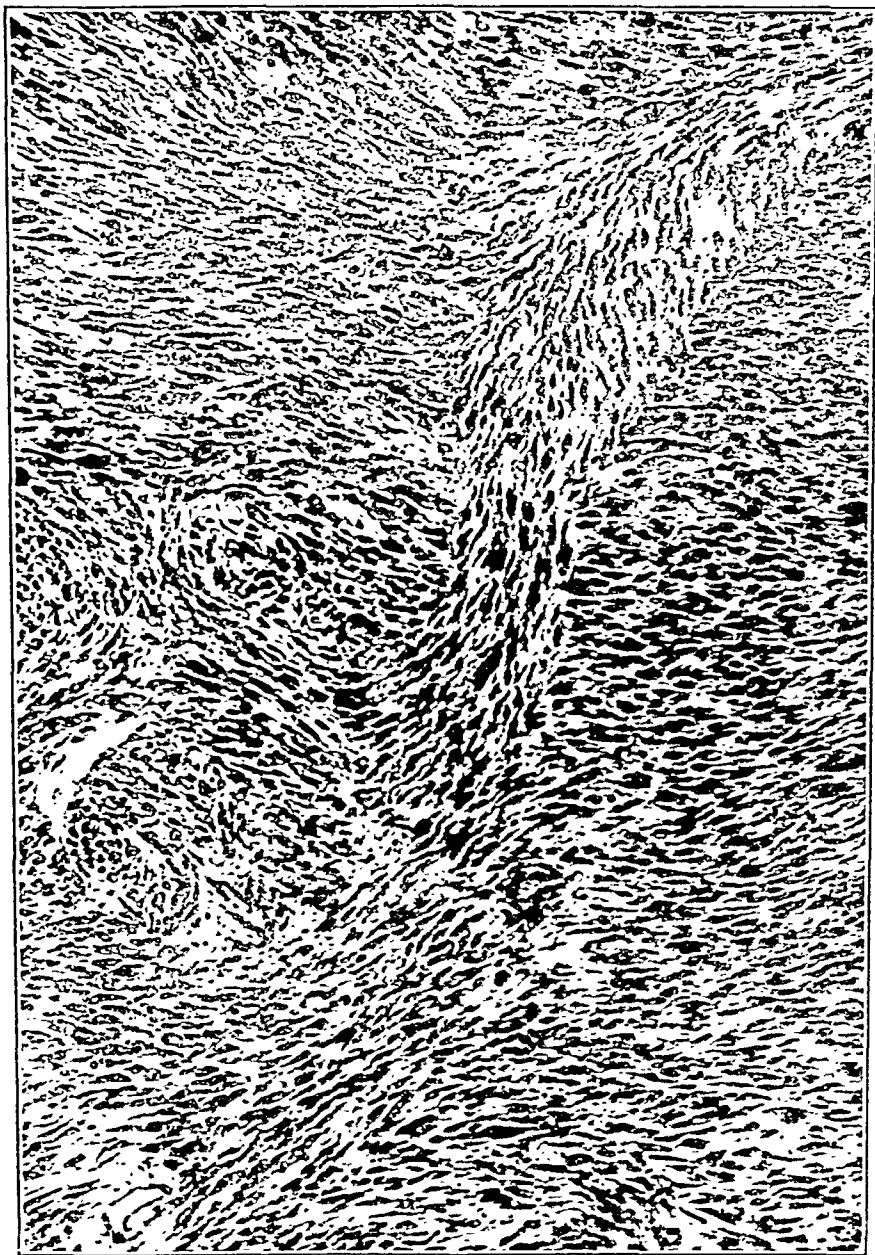


Fig. 7.—Low power photomicrograph of a section taken from the tumor involving the femur. Notice the interlacing bundles of spindle-shaped cells and the variation in shape and in density of staining of the nuclei.

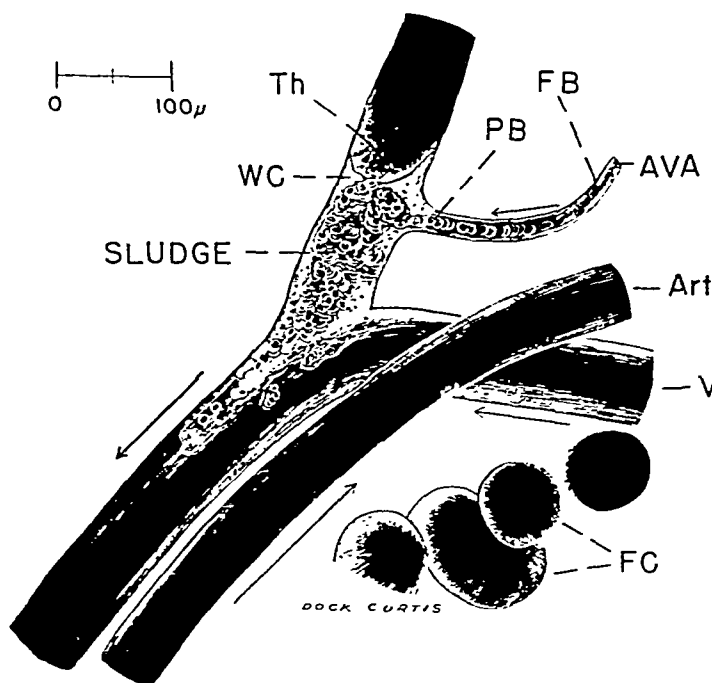
There was palisading of the nuclei. In the entire section, the tissue was more cellular and less uniform in structure than in the ordinary benign leiomyoma. The nuclei in many areas showed inequality in size and variation in shape and in density of staining. Irregular pyknotic masses of nuclear substance were observed in large numbers, but comparatively few clearly defined

Subsequent roentgenologic examinations of the region of the left hip showed (figs. 3, 4 and 5) progressive damage and destruction of the head and neck of the left femur. Additional films of the chest showed no evidence of pulmonary metastases.

The patient's course continued to be septic; she rapidly lost weight; a large severe decubitus ulcer

significantly, probably because all the vessels of the area were by microscopic standards fairly large; arterioles, arteriovenous anastomoses and venules of this size have substantial smooth muscle coats.

6. At the moment the finger was removed from the tissue, few if any white cells were sticking to the walls of injured vessels. However, many of those brought in by the flowing blood adhered to the injured walls. Hence, in a few moments white cells had accumulated one or two and even three layers deep and in irregular masses on injured endothelial surfaces (see the figure and consult E. R. and E. L. Clark<sup>10</sup>).



Ciné-tracing of a motion picture of blood flowing through crushed monkey omentum. *Art*, artery; *V*, vein; *AVA*, arteriovenous anastomosis; *FC*, fat cells; *Th*, thrombosed venule; *WC*, masses of white cells stuck on inner surface of injured venule; *FB*, fluid blood; *PB*, precipitated blood, and *SLUDGE*, masses of precipitated-agglutinated blood. Note the scale in upper left. Arrows show direction of blood flow. The details of the precipitated-agglutinated blood were added by the artist while studying a looped continuous projection of the scene.

The adhering masses of white cells were continually being bumped by wads of the rapidly moving sludge; from time to time masses of these white cells were forced loose from the vessel lining and carried downstream to the general circulation.

This microscope field was then photographed on Kodachrome motion picture film at 24 frames per second and a Zeiss microscope scale photographed with the same lens combination, in order (a) to measure the dimensions of the structures present, (b) to find out how long it was taking fluid blood to change to thick pasty blood, i. e.,

to determine the precipitation rate (Nygaard<sup>29</sup>), and (c) to record the scene for further study. The scene is somewhat underexposed, satisfactory for research purposes or private showing but not for general distribution.

Copies of this film were later spliced into loops for continuous projection to permit several persons to study the scene together, repeatedly, detail by detail. The outline of the figure is a ciné tracing of the scene, made by projecting the film onto a large sheet of drawing paper while an artist traced the outlines of the stationary structures (Brown and Sheard<sup>30</sup>). Thus these outlines and the scale have about the same accuracy as a good camera lucida drawing. The

following additional results were obtained from studies of the film.

7. The blood was fluid at point *FB* and rather solidly precipitated at *PB*. The precipitation end point is not exact, however, nor exactly determinable from the scene. Nor was the precipitation rate constant. Sometimes fairly solid precipitates were formed in blood which had

29. Nygaard, K. K.: Hemorrhagic Diseases—Photo-Electric Study of Blood Coagulability, St. Louis, C. V. Mosby Company, 1941.

30. Brown, G. E., and Sheard, C.: Measurements of the Skin Capillaries in Cases of Polycythemia Vera and the Role of These Capillaries in the Production of Erythrosis, *J. Clin. Investigation* 2: 423 (June) 1926.

Operation was indicated in this group of 9 cases by the evidence of acute cord compression and the failure to demonstrate a primary lesion. Preoperative study was limited to complete history, physical examination and roentgen ray examination of the chest. The effects of the cord compression were generally unrelieved by operation, but the pain was alleviated in the majority of cases by the decompression afforded the spinal roots.

The tumors grossly were all extremely friable and encircled the dura both anteriorly and posteriorly. The laminae and the spines were always more extensively involved than the roentgen ray picture would lead one to believe. Microscopically the tissue was easily identified, although in several cases necrosis was so pronounced that histologic diagnosis rested on relatively small intact portions about the periphery of the lesion. Five of the lesions were adenocarcinomas, two were squamous cell epitheliomas and two were undifferentiated.

#### MYELOMAS

The lesions in this series that proved to be myelomas were associated with a uniform clinical picture. The patients were in the fifth to seventh decades of life, and all complained of an abrupt onset of symptoms of cord compression (three days to three months). There was roentgen evidence of vertebral erosion, usually in the thoracic region, and all patients had complete spinal subarachnoid block when tested by the Queckenstedt maneuver and/or by myelography after injection of iodized poppyseed oil (table 3). Six of the seven myelomas occurred in men. The acute onset of cord compression, preceded perhaps by a few months' history of localized root pain, was the first evidence of this usually widespread disease. In many instances, the exigencies of the acute cord compression compelled operation before complete roentgenologic studies of the skeletal system had been made. However, in the only 2 patients completely studied preoperatively (cases 12 and 15), the vertebral lesion causing the compression was an isolated one. One of these patients died three months postoperatively, without evidence of other involvement (case 15), but the other showed roentgenographic evidence of rib involvement four months after operation (case 12). Three patients were not sufficiently studied at any time prior to or after death to allow us to state whether the lesion of the vertebra was solitary or not. In the remaining 2 cases, other scattered lesions were demonstrated before the

patients were discharged from the hospital. Alterations in the serum proteins and presence of Bence-Jones protein in the urine were not observed in the 3 cases in which appropriate laboratory examinations were done (cases 11, 12 and 14).

The epidural mass found at operation was usually described as extremely vascular and ringing the dural sac. However, in 2 instances the lesion was entirely anterior to the dura, the dural sac and cord knuckling over the mass. The tumors were composed of closely packed masses of cells which resembled plasma cells, although varying degrees of pleomorphism were observed. The resemblance to plasma cells was always sufficiently pronounced for ready identification. As a group these patients succumbed rapidly, the longest survival being fourteen months. One patient is still alive, having survived operation for one year.

The age and sex incidence in our small group is in accord with that noted in the literature.<sup>2</sup> The vertebrae are among the more commonly involved bones (Ewing<sup>3</sup> and Geschickter and Copeland<sup>4</sup>). Denkes and Brock<sup>5</sup> emphasized the frequency of neurologic signs and called attention to a group of patients who presented paraplegia as an initial symptom. According to these authors, the thoracic vertebrae are the ones most frequently involved. Davison and Balser<sup>6</sup> have reported 6 cases in which there were spinal involvement and cord compression.

Willis<sup>7</sup> has emphasized the rarity of solitary myelomas as compared with multiple lesions. He stated that of those which appear solitary when they first come under observation a number will subsequently become multiple, usually within the first year. Three of our patients are known to have multiple lesions. We cannot be certain of the solitary nature of the myeloma in the other 4 cases because clinical study was incomplete. Furthermore, Sproul<sup>8</sup> has pointed out

2. Atkinson, F. R. B.: Multiple Myelomata, M. Press 195:312, 1937.

3. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940, p. 328.

4. Geschickter, C. F., and Copeland, M. M.: Tumors of Bone, New York, American Journal of Cancer, 1936, pp. 448-449.

5. Denkes, P. G., and Brock, S.: The Generalized and Vertebral Forms of Myeloma: Their Cerebral and Spinal Complications, Brain 57:291, 1934.

6. Davison, C., and Balser, B. H.: Myeloma and Its Neural Complications, Arch. Surg. 35:913 (Nov.) 1937.

7. Willis, R. A.: Solitary Plasmocytoma of Bone, J. Path. & Bact. 53:77, 1941.

8. Sproul, E. E.: Multiple Myeloma, in Nelson's Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1941, vol. 4, pp. 91A-91GG.

4. For a time after the crush, the rate at which sludge is poured into the venous system can be as fast as the rate of flow through an open vessel in the crushed area.

5. This sludge can be formed in an area from which or into which there is (a) no hemorrhage and (b) but little loss of plasma through injured vessel walls.

6. When first formed, some of the masses have sufficient internal rigidity to bulge the walls of the vessel through which they are being forced; if not changed, such masses would resist passage through capillaries.

7. When first formed, the outer surfaces of the precipitated material are sticky to each other; hence, if not changed, masses coated with this material must, whenever they touch each other, tend to stick together and form larger masses.

8. The precipitated material contains erythrocytes and may be ingestible by the phagocytes of spleen, bone marrow and liver. If the material is phagocytosed, the contained erythrocytes would be removed from the circulatory system and destroyed.

*Working Hypothesis.*—Putting these bits together, one can formulate a working hypothesis about mechanisms which might cause death after crushing injuries. This hypothesis can perhaps best be stated as a set of general questions, as follows:

1. Can the crushing of tissues cause the release of substances from the crushed tissues which can cause the precipitation and agglutination of blood flowing through or beside the crushed tissues?

2. Can the crushing of gross regions of the human body or of specific tissues or organs initiate processes which can change all the circulating blood to a sludge whose masses are large enough and rigid enough to retard the flow in small vessels enough to cause them to become anoxic and leak?

3. From crushing injuries alone, can the circulating blood be changed to a sludge which resists flow through small vessels enough to cause rapid local fluid losses all over the body, plugging of vessels with agglutinated masses, decreasing circulating blood volume, failure of venous return and death?

4. Following trauma, does rapid ingestion of coatings containing red cells by the phagocytes of liver, bone marrow and spleen (a) contribute to decreasing the total numbers of circulating red cells and (b) assist in causing progressively decreasing circulating blood volume?

5. In many injuries, hemorrhage and trauma are of course both present. Can these sludge mechanisms contribute to the decreased venous return in animals and human patients who have suffered combinations of hemorrhage and trauma?

These five questions define the broad outlines of the problem. Note that the questions deal with (a) concepts of chemical reactions, (b) concepts of degree and (c) concepts of rates. The rest of this paper is an attempt to find the beginnings of the answers to the first of these questions.

*Reflections About the First General Question.*—Consider the first general question in the aforementioned series. Obviously this question needs subdividing, for it contains or implies questions such as these:

Are the precipitation and agglutination of the blood flowing past the injury due to the liberation of one or more diffusible substances from injured tissues? Is the same diffusible substance released from each crushed tissue? What factors determine the rates of release of the diffusible substances? If such diffusible substances are released from injured tissues, do they always react and then become inactive at or very near the site of injury, or may they be carried in the circulating blood for a time and act later, after they have accumulated to or above some threshold concentration? That is, may some one or more of such diffusible substances act immediately and some accumulate in solution in the circulating blood for a time after an injury and later initiate changes in the mechanical consistency of the circulating blood?

These questions cannot at present be tested directly, but, as a first step in finding the answers to them, the following questions can be asked, each of which can be tested by direct methods.

(a) Which tissues or organs cause sludging of the blood after they are crushed?

(b) What are the characteristics of the sludge produced by the crushing of each tissue? Are the sludges thus produced alike or visibly different?

(c) How slight an injury causes sludging of the blood passing the injured area?

(d) What degree of severity of injury is present after tissue is crushed? What happens after each?

(e) For how long a time after a tissue is crushed does the sludging of the blood continue? What factors determine the duration of this process?



## GIANT CELL TUMOR OF BONE

The clinical picture presented in the 3 cases in this group was remarkably consistent. The patients were in the second decade of life, and the onset of cord compression was relatively abrupt (table 5). Pain in the back had been present for a matter of months, but the duration of cord compression was given as six weeks, four weeks and two days, respectively, and progressed rapidly. The lesions were all thoracic in location, and the roentgenograms showed erosion of the spines, pedicles and/or bodies of the vertebrae. There was no history of trauma. The occurrence of such lesions in the vertebrae of young persons is the subject of a number of reports in the literature, as is the relatively rapid progress of cord compression, which is seen to some degree in about 50 per cent of cases. The site, however, is not limited to the dorsal area but is well

Lewis.<sup>14</sup> The frequency with which spindle cells predominate in the giant cell tumors of the small bones, especially the vertebrae, has been pointed out by Geschickter and Copeland,<sup>15</sup> who expressed the opinion that it, along with the new bone formation, is evidence of a healing reaction. Although not conspicuous, this feature is seen in our cases. These variations of the giant cell tumor of small bones from the typical epiphyseal giant cell tumor—the frequent finding of new bone formation, the predominance of spindle cells and the age distribution—all suggest a relationship to bone cyst. Our cases are representative of the usual age distribution of vertebral giant cell tumors, whereas giant cell tumors of other situations commonly occur at a later age.<sup>16</sup> Most authors are agreed that the giant cell tumor of the spine is benign,<sup>17</sup> and Geschickter and Copeland stated<sup>15</sup> that it has

TABLE 5.—Giant Cell Tumor of Bone (5.6 per Cent)

Case No.	Age, Yr.	Sex	Duration of Pain	Duration of Cord Compression	Roentgenogram of Spine	Location of Epidural Lesion	Roentgen Ray Therapy	Result
23	10	F	2 mo.	1 mo.	Erosion vertebral body and facets T-5	T-5	Two courses, 1 wk. and 3 mo. postoperatively (amount of roentgens not known)	Well, 9 yr.
24	20	F	4 mo.	2 days	Erosion spines and pedicles T-4 and T-5	T-3 to T-5	2,100 r 2 mo. postoperatively (in one course over 1 mo. period)	Well, 2 yr.
25	15	M	9 mo.	6 wk.	Erosion pedicles T-6 and T-7	T-7	Incomplete course of 200 r 2 weeks postoperatively	Well, 3½ yr.

distributed throughout the entire length of the vertebral column.

The operative findings were similar in each case. An encapsulated epidural tumor mass was found, its bulk posterior to the dural sac, but with a tendency to extend forward about the dura in the lateral gutters of the intravertebral canal. Connection with the bony defects seen on roentgenographic examination was not remarked on. On section, red soft granular but not friable tissue was seen to lie between fibrous bands.

The tumors were composed of giant cells scattered in varying numbers in a vascular and cellular stroma (fig. 2). The giant cells were of the type commonly seen in giant cell tumors of bone, generally with numerous small, ovoid nuclei. The stromal cells were of moderate size and either rounded or spindle shaped. In 1 of our cases there were extensive areas of hemorrhage and the giant cells were relatively infrequent. The sections of two of the lesions showed extensive new bone formation, a feature of the vertebral giant cell tumor emphasized by Dean

even less tendency to recur than do giant cell tumors in other locations. All 3 of our patients are well after surgical curettage and postoperative irradiation after two, three and a half and nine years respectively.

## MISCELLANEOUS EPIDURAL TUMORS

*Lymphosarcoma.*—There were only 2 cases of lymphosarcomas in our series, although several other cases had been previously so classified

14. Lewis, D.: Primary Giant Cell Tumors of the Vertebrae, J.A.M.A. **83**:1224 (Oct. 18) 1924.

15. Geschickter and Copeland,<sup>4</sup> pp. 333-341.

16. Willard, deF., and Nicholson, J. T.: Giant Cell Tumor of the Cervical Spine, Ann. Surg. **107**:293, 1938.

17. Santos, J. V.: Giant Cell Tumor of Spine, Ann. Surg. **91**:37, 1930. Grieve, W. E.: Giant Cell Tumor of Vertebrae, Northwest Med. **33**:81, 1934. MacFarlane, J. A., and Linell, E. A.: Benign Giant-Cell Tumor of Third Cervical Vertebra, Brit. J. Surg. **21**:513, 1934. Murphy, G. W.: Giant Cell Tumor of Spine, Am. J. Roentgenol. **34**:386, 1935. Duncan, G. A., and Ferguson, A. B.: Benign Giant Cell Tumor of the Fourth Lumbar Vertebra, J. Bone & Joint Surg. **18**:769, 1936. Giant Cell Tumor of Spine, Cabot Case 23081, New England J. Med. **216**:348, 1937.

At 6 p. m., ninety minutes later, the following observations were made: 1. The plugs were still present in the two thrombosed venules. 2. The damaged area was still pouring sludged blood into the smaller veins which drained it. A point was found where a venule which came from the damaged area joined one which came from an area of undamaged muscle. Here the experiment and the control were present in one microscope field; it was easy to compare the sludged and the normal blood. There were no free individual cells in the blood passing out of the venule draining the damaged area; all this blood was precipitated and agglutinated into a sludge. 3. No two red cells were sticking together in the blood from the uninjured area; all were free, each turned over by itself unattached to any other—that is, normal blood was flowing through normal vessels in adjacent untraumatized areas of the muscle.

At 6:15 p. m. blood passing through the injured area was still changing to a sludge. At this time, however, there began to be a change. Some of the smallest venules in the injured area had almost normal blood for a few minutes and then sludged blood again. The sludge was being formed intermittently, and the sludge being formed was softer, i. e., the clumps had a fluffy, feathery character rather than a firm, rigid texture. The area was still pouring sludge into the venous system, but there had been a definite decrease in rate of production of sludge, and that produced might better be called a "slush" than a sludge.

It seems reasonable to assume that whatever had been initiating the production of sludge was not reaching or acting in the blood flowing through the injured area as rapidly as during the first ninety minutes after injury.

At 6:30 p. m. the following observations were made. 1. The plugs were still present in the two thrombosed venules. 2. The blood flowing through the injured area was still changing consistency. The sludge formed was less pasty than that formed at first. It was softer, the clumps were more plastic and the rates of flow through these vessels were increasing, approaching the rates through vessels of similar size in the neighboring undamaged areas. The walls of the venules in the injured area were lined with sheets of white cells all rolling along the inner surfaces of the endothelium (E. R. and E. L. Clark<sup>10</sup>). It seemed probable that this injured area would not form sludge much longer. 3. Normal, unagglutinated blood was coming from the uninjured areas.

At 7:30, three hours after the injury, these observations were noted: 1. The two venules originally thrombosed were still plugged up. 2. Patches of slightly agglutinated blood were forming at irregular intervals in blood flowing through the injured area. 3. Normal blood was coming out of the uninjured areas.

At 7:40 the same area was retraumatized by one light wiping stroke of the forceps handle. Immediately the blood flowing through the area became thick and pasty again. This shows that the substances which initiate sludge formation, or their precursors, were not all gone from the injured area.

At 7:55 p. m. the following observations were made: 1. Thrombosed vessels were still thrombosed. 2. Blood flowing through the injured area was still changing to a stiff sludge. 3. Normal blood was coming out of venules of neighboring uninjured muscle.

At 8:15 p. m. there was no change.

At 8:40 p. m. these observations were made: 1. Thrombosed vessels were still thrombosed. 2. All the blood flowing through the injured area was changing to a sludge and passing into the venous system. 3. Normal blood was coming from uninjured areas. The experiment was discontinued.

*Summary of This Experiment with Crushed Mouse Muscle.*—1. A light injury to mouse striated muscle caused precipitation and agglutination of the blood flowing through the injured area. Crush and flow through the crushed muscle were both necessary, and the two together were sufficient to produce a flow of sludged blood into the general circulation.

2. The precipitate was probably being formed in less than half a second.

3. For about one and three-fourths hours after the injury, the rate at which sludged blood was poured into the venous system was as fast as the rate of flow through the crushed area.

4. For the next one and one-fourth hours a progressively decreasing fraction of the blood flowing through this area changed consistency.

5. The clumps formed in the first period were fairly tough and rigid; those formed in the second period were increasingly plastic, flexible and fragile.

6. The visible sludge formed rapidly before the blood left the field being observed. This observation does not mean that all the sludge initiator substances reacted and became inactive within the microscope fields observed. Initiator substances which might be able to cause changes in the blood at some later time and distant place

series, however, there is only 1 example of this lesion, although 1 of our unclassified cases may represent a second. The patient was a 54 year old spinster who had gradually progressive weakness of the lower limbs over a period of one year. She did not experience symptoms of root irritation at any time. A roentgenogram of the thoracic portion of the spine revealed erosion of the body of the fourth thoracic vertebra that was interpreted as typical of angioma. Operation revealed a bright red, encapsulated, extremely vascular extradural lesion measuring 3 by 1.5 by 2.5 cm. and weighing 2.5 Gm. Histologically, it was a characteristic cavernous hemangioma. After its removal the patient made a full recovery, and when last heard from, three years after operation, she was gainfully employed and her only residuum was occasional girdle-like pain.

We have observed one other extradural vascular tumor in this series. This was a metastatic tumor of an unusual type occurring in a 43 year old man who had complained for five months of pain in the back. He had had progressive weakness of the legs for one month. Roentgenologic study of the spine revealed a destructive lesion of the third thoracic vertebra. At operation the laminae of the second, third and fourth thoracic vertebrae were extremely friable and highly vascular, and the epidural space was filled with a red, soft, friable, vascular tumor. This man had been admitted to the hospital on eleven previous occasions, every time but one for study and treatment of disease conditions unrelated to the present complaints. However, two years before the onset of cord symptoms, he had been hospitalized for surgical removal of a tumor of the soft tissues of the thigh. This tumor never recurred locally. During convalescence from laminectomy a discrete pulsating mass became apparent over the sternum, and roentgen ray examination demonstrated involvement of the underlying bone. The patient's condition was not improved by operation, and he died five months

later in another hospital. Autopsy was not performed.

The tumor was composed basically of small capillaries lined by normal-appearing endothelial cells and surrounded and supported by a dense network of collagen and reticulin fibers (fig. 4). The tumor cells, which were usually rounded or ovoid but occasionally elongated, were massed outside the reticulin fibers which immediately surrounded the vessels, an arrangement well demonstrated only by silver reticulin stains. In general, the vessels were so close together that the cells surrounding one vessel merged with those surrounding others. There was a moderate degree of cellular pleomorphism, and occasional mitotic figures were seen.

We were privileged to study the sections of the tumor removed from the thigh two and one-half years before. It was strikingly similar to that removed from the epidural space, but the fundamental structure was somewhat more readily apparent in the primary tumor. This structure, "basic composition of endothelium-lined capillaries or impervious endothelial sprouts surrounded by rounded cells with a supporting meshwork of reticulin fibers," is described by Stout and Murray<sup>22</sup> as characteristic of the tumor which they have labeled "Hemangiopericytoma." Most of the 9 tumors they reported on and the hemangiopericytoma of the omentum subsequently described by Stout and Cassel<sup>23</sup> were benign, but the group reported by Stout and Murray included one tumor which exhibited aggressive, infiltrative local growth and one example of a malignant metastasizing neoplasm (case 9). The latter tumor arose in the soft tissues of the thigh of a 34 year old Negro woman and seven years later (four years after excision) multiple metastases to the liver were demonstrated at laparotomy and verified by biopsy. Later roentgenographic evidence of metastases in two ribs developed, and she finally died three years after the demonstration of hepatic involvement. In addition to the features characteristic of hemangiopericytoma, her tumor showed areas where extensive fibrosis and hyalinization had taken place about the vessels, pushing aside the pericytes, which appeared atrophic. Some areas in the tumor observed by us closely resembled this picture.

We have classified our case as an instance of a malignant hemangiopericytoma, primary in the

8) 1938. Karshner, R. G.; Rand, C. W., and Reeves, D. L.: Epidural Hemangioma Associated with Hemangioma of the Vertebrae, *Arch. Surg.* **39**:942 (Dec.) 1939. Kelly, L. C.: Vertebral Hemangioma with Neurologic Symptoms, *New York State J. Med.* **40**: 1607, 1940. Turner, O. A., and Kernohan, J. W.: Vascular Malformations and Vascular Tumors Involving the Spinal Cord, *Arch. Neurol. & Psychiat.* **46**: 444 (Sept.) 1941. Ghormley, R. K., and Adson, A. W.: Hemangioma of Vertebrae, *J. Bone & Joint Surg.* **23**: 887, 1941. Ferber, L., and Lampe, I.: Hemangioma of Vertebra Associated with Compression of Cord, *Arch. Neurol. & Psychiat.* **47**:19 (Jan.) 1942. Blackford, L. M.: Hemangioma of Vertebra with Compression of Spinal Cord, *J. A. M. A.* **123**:144 (Sept. 18) 1943.

22. Stout, A. P., and Murray, M. R.: Hemangiopericytoma: A Vascular Tumor Featuring Zimmermann's Pericytes, *Ann. Surg.* **116**:26, 1942.

23. Stout, A. P., and Cassel, C.: Hemangiopericytoma of the Omentum, *Surgery* **13**:578, 1943.

pattern of the injury determine (a) the total volume of injured tissue and (b) the relative proportions of the thrombosed and partially crushed or sludging zones.

The amount of partially crushed tissue varies from injury to injury, but in each case it is the partially crushed tissue which pours sludge into the venous system. The amount of such partially crushed tissue present after an injury depends on the size and shape of the instrument, on the pressure applied and on the size and shape of the structures which supported the injured tissues.

From these observations, it seems probable that when they are crushed striated and smooth muscles release substances capable of diffusing in through the vessel walls and reacting with constituents of the blood flowing through the patent vessels.

From the observations it seems probable that the maximum amounts of initiator substances reach the blood from partly crushed tissue, that is, from regions injured enough to release the initiator substances but not injured enough to thrombose the enclosed vessels. The edge of a thrombosed region may of course be contributing initiator substances to a contiguous partly crushed region.

The sludge formed at the site of the injury is formed rapidly, before the blood leaves the field being observed, but this does not mean that all the sludge formed necessarily is formed at the site of the injury. Excess initiator substances which might be able to cause changes in the blood at some later time and distant place may well be being carried out of view into the general circulation. The observations reported thus far were made in mammals, but some observations made in amphibians (frogs and salamanders) may have a bearing on this point. In these animals an extensive operation done with care to prevent loss of blood (Kniseley, Bloch and Warner<sup>24</sup>), but without care to prevent partial crushing of tissues at the edges of incisions, is often followed by a slow increase in the viscosity of the plasma of all the circulating blood. In these animals a visible sludge may or may not form at the sites of injury. It seems reasonable to assume that in these amphibians initiator substances are carried into the general circulation before producing a visible change in the blood. Hence, by analogy it seems possible that in mammals excess initiator substances released at the sites of injury are being carried out of view into the general circulation. Such substances could cause further changes in the circulating blood and/or help bind masses of

sludge together into larger masses whenever they accumulate to or above some threshold concentration. This is not altogether an academic speculation; it may have a practical aspect, for transfusions given animals or men during or after the accumulation of such substances in the circulating blood must, among other things, dilute the initiator substances.

It seems reasonable to suspect that the initiator substances might be related to the substances capable of initiating blood clotting. If this is true, then sludge initiator substances should be released from many different injured tissues and organs of vertebrates.

The outer surfaces of the erythrocyte-containing masses formed in blood flowing through crushed tissues are not conspicuously different either in appearance or in observed behavior from the coated, red cell-containing masses formed in monkeys with *P. knowlesi* malaria. Hence, (a) the *P. knowlesi* malaria precipitates should be examined both chemically and immunologically to determine whether they are monkey fibrin or related to fibrin and (b) the precipitated coatings with their contained red cells formed in blood flowing through crushed tissues may be ingestible by phagocytes of spleen, bone marrow and liver. In monkeys with malaria, this mechanism destroys blood rapidly (Kniseley, Stratman-Thomas, Eliot and Bloch<sup>6</sup>). Thus the phagocytosis of coated red cells may well contribute to the removal of blood from the vascular system after a traumatizing injury and to the anemia which not infrequently follows operations (Kniseley, Bloch and Warner<sup>24</sup>).

A bit of sludge can reach the general circulation only by being carried into the venous system. Hence sludged blood can come from one minute injured area into the general circulation no faster than the flow through the venules which drain the injured area. These facts are important when one is considering the mechanisms of the crush syndrome (review and bibliography by Bywaters<sup>25</sup>).

The volume of sludge produced by the partially crushed area drained by one small venule may be expressed as the summation of volumetric rates of flow through the venule during the periods while sludge is produced. Hence, by induction, the amount of sludge produced by any partially crushed area is equal to the summation

38. Bywaters, E. L. G.: Ischemic Muscle Necrosis: Crushing Injury, Traumatic Edema, the Crush Syndrome, Traumatic Anuria, Compression Syndrome; a Type of Injury Seen in Air Raid Casualties Following Burial Beneath Debris, *J. A. M. A.* **124**:1103 (April 15) 1944.

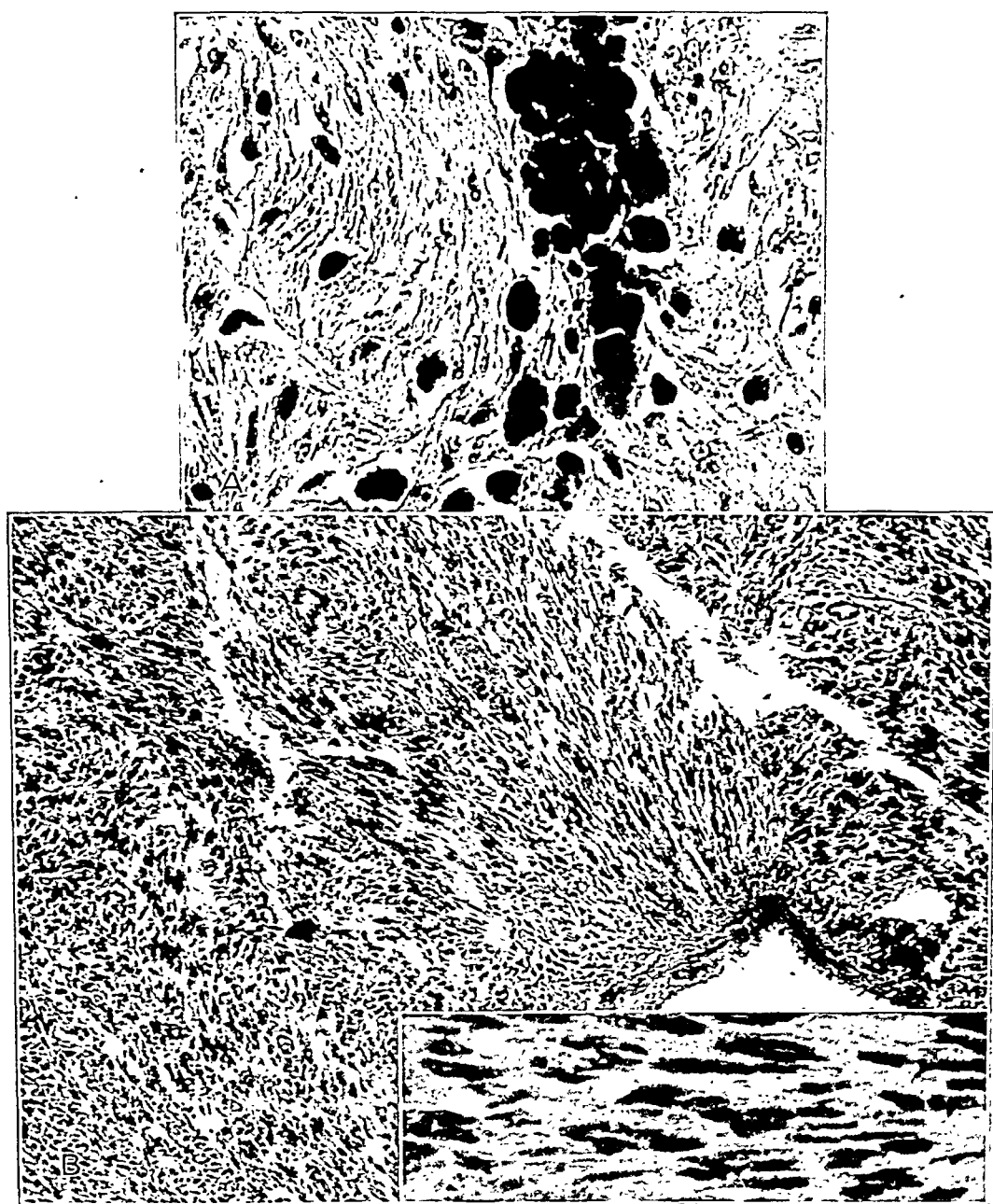


Fig. 6.—Unclassified tumors of spinal epidural space. *A* (above), case 34. Hemangioma? after irradiation. The large cells with occasional eosinophilic intranuclear inclusions can be seen, although hemosiderin deposition is the most conspicuous finding. Hematoxylin and eosin;  $\times 260$ . *B* (below), case 35. Malignant neurilemmoma? The photomicrograph is of a metastatic nodule in the lung. The nuclear palisading is strongly suggestive of nerve sheath origin. Palisading was not seen elsewhere in numerous sections of both the primary tumor and the metastases. Hematoxylin and eosin;  $\times 132$ . Inset shows detail.  $\times 600$ .

capillary venules and venules do not leak enough to be detected by microscopic observation.

4. Pentobarbital sodium in anesthetic doses does not cause intravascular agglutination of the circulating blood of *Macacrus rhesus* monkeys.

5. Neither pentobarbital sodium nor sodium amytal in anesthetic doses causes intravascular agglutination of the circulating blood of mice.

6. No single factor or combination of factors of the anesthetics used, the withdrawing of the monkey omentum or the brilliant transillumination of tissues whose temperatures are maintained at normal has caused intravascular agglutination of the blood.

7. Laparotomies can be done with sufficient care to prevent general precipitation and agglutination of all the circulating blood.

8. With routine care, normal monkeys have been kept under pentobarbital sodium anesthesia and the circulation in abdominal viscera observed with microscopes without causing general intravascular agglutination of the blood or visible pathologic changes in the walls of small blood vessels for as long as fourteen to eighteen hours.

*II. Methods.*—1. A method is described for maintaining controlled pentobarbital sodium anesthesia of monkeys by intrapleural injections; this is useful for making microscopic observations of abdominal structures.

2. Simple methods are described for studying the vessels and blood of the eyelid, nictitating membrane and bulbar conjunctiva of experimental animals not operated on and of those operated on. The methods have three obvious uses:

(a) To assist in preselecting normal animals for experiments. As agglutinated blood is not normal, as agglutinated blood has already been found as a part of the pathologic change in about forty human diseases and as many of the organisms which affect human beings also affect experimental animals, microscopic observations of the blood and vessel walls are a necessary part of the preselection of normal animals for experiments.

(b) To make continuous observations during the course of experiments on intact animals not operated on to determine the effects of various agents and procedures on the circulating blood and local vessel walls.

(c) To make continuous observations as controls to be certain that during experiments designed with the intention of studying normal animals no agent or procedure is causing mechanical changes in blood and/or pathologic changes in vessel walls.

3. A method is described for studying the blood passing through vessels in or near a minute local lesion. The method should be useful for studying the blood passing through or near lesions caused by many different agents.

*III. Results of Crushing Injuries.*—1. After a crushing injury to monkey omentum, smooth muscle of mouse intestine or striated muscle of a mouse, three zones may be distinguished: (a) a thrombosed zone, (b) a partially crushed or sludging zone and (c) a zone which is injured so little that the blood flowing through it undergoes no detectable change.

(Pentobarbital sodium in monkeys and mice and sodium amytal in mice do not in anesthetic doses prevent the precipitation-agglutination of blood flowing through a crushed area.)

Seen as possible initiating factors in traumatic shock, the observations made in these tissues may be summarized as follows:

2. Crushing plus flow through a vessel in the crushed area yields a stream of sludge into the general circulation.

3. Crushing plus thrombosis of a crushed vessel yields no sludge to the venous system.

4. Flow without crush yields no sludge.

5. Thus, after trauma, (a) local crush plus (b) flow through a vessel in the crushed area are both necessary and, together, sufficient to yield a flow of sludged blood into the general circulation.

6. After crush, precipitates can form around or between the moving blood cells in less than a second, while the blood is moving less than a millimeter.

7. It seems reasonable to suspect that the sludge initiator substances might be related to the substances capable of initiating blood clotting. If this is true, then many tissues and organs of vertebrates should release such substances when they are injured.

8. At no time can sludged blood pass into the venous system faster than the flow through the crushed tissue.

9. For a time after the crush, the rate at which sludge is poured into the venous system can be as fast as the rate of flow through an open vessel in the crushed area.

10. Retraumatization of an area can reinitiate sludge formation in blood flowing through the area.

11. This sludge can be formed in an area from which or into which there is (a) no hemorrhage and (b) but little loss of plasma through injured vessel walls.

d three months postoperatively of generalized sis. Three patients are still alive; 1 is able get about on crutches, but sphincter function still absent after six years; another, one and

one-half years after operation, has shown pronounced recovery, getting about with a cane, performing his usual sedentary job and enjoying satisfactory control of the bladder. The last

TABLE 9.—Epidural Infections Processes: Acute Suppuration (11.1 per Cent)

se; A; re, r.	Dura- tion of Pain	Duration of Cord Com- pression	Roentgen- ogram of Spine	Level of Lesion	Evidences Sources of Infection	Result	Comment
Acute Suppuration (11.1 per cent)							
11 F 12	8 days	18 hr.	Normal	C-3 to L-3	Injured back in auto- mobile accident 10 days previously	Died 1 hr. postopera- tively of respiratory paralysis	Hemolytic Staphylococcus aureus cultured
12 M 15	2 wk.	1 wk.	Normal	D-4 to L-4	Infected finger 1 mo. prior; incision and drainage 2 wk. prior	Able to get about on crutches; automatic bladder 6 yr. postoper- atively	Hemolytic Staph. aureus cultured
43 M 50	3 wk.	2 days	Normal	T-4 to T-6	Furuncle finger 1½ mo. prior; incised several times	Died 19 days postopera- tively of coronary or pulmonary occlusion	Hemolytic Staph. aureus cultured
44 F 49	2 wk.	4 days	Normal	T-8 to T-10	Draining sinus left thigh, 3 yr. duration	Died 3 mo. postopera- tively of generalized sepsis	Hemolytic Staph. aureus cultured
45 M 16	2 wk.	2 wk.	Normal	T-2 to T-7	Thrombophlebitis left leg, 7½ yr. of age; pyarthrosis left hip at 10 yr. of age; sinusitis with frontal osteomyelitis at 14 yr.; furuncle on neck 3 wk. prior to epidural abscess	Unimproved 6 mo. post- operatively; not heard from since	Hemolytic Staphylococcus albus cultured
46 M 30	2 wk.	2 wk.	Normal	L-1 to L-5	Appendix removed with patient under spinal anesthesia 4 days prior to onset; two furuncles on hand 3 to 4 wk. prior to onset	Coronary occlusion 1½ mo. postoperatively; walking with cane and back at work (office) 1½ yr. postoperatively	Hemolytic Staph. aureus cultured
Chronic Nonspecific Granuloma (5.6 per cent)							
47 F 18	8 mo.	1 mo.	Normal	C-2 to C-4	Pharyngitis and tonsil- lectomy 4 mo. prior to symptoms	Neurologically normal 10 yr. postoperatively	No culture taken
48 F 55	1 yr.	2 wk.	Normal	T-11 to T-12	None ascertained	Spinal shock postopera- tively; died of urinary sepsis and debility 1½ yr. later without functional improvement	No culture taken
49 M 67	2 yr.	2 yr.	Old com- pressed frac- ture T-5 vertebra	T-7 to T-8	None ascertained	Unimproved; died 1½ mo. later of generalized sepsis	No culture taken
Syphilitic Granuloma (5.6 per cent)							
50 F 33	6 wk.	3 wk.	Normal	T-3 to T-7	Blood and spinal fluid serologic reactions 4 plus	Neurologically normal 10 yr. postoperatively	Adequate antisyphilitic roentgen ray treatment postoperatively; severe direct trauma to upper thoracic area 2 days before onset of pain
51 M 28	5 mo.	4 mo.	Erosion of verte- bra T-5	T-4 to T-7	Blood and spinal fluid serologic reactions 4 plus	Neurologically normal 4 yr. postoperatively	Adequate antisyphilitic roentgen ray treatment postoperatively; indirect trauma to upper thoracic area 1 mo. prior to onset of symptoms
52 M 50	7 mo.	5 days	Roentgen- ograms unsatis- factory	T-2 to T-5	Reaction to Wassermann test of blood 4 plus; spinal fluid anticomple- mentary; chancre 20 yr. before	Neurologically normal 2 yr. postoperatively	Adequate antisyphilitic roentgen ray treatment postoperatively; severe direct upper thoracic trauma 8 mo. prior
Tuberculous Granuloma (3.7 per cent)							
53 M 25	5 mo.	2 mo.	Normal	T-4 to T-6	Roentgenogram of chest; bilateral inactive tuberculosis	Improved; able to walk with cane 2 yr. post- operatively	Laminectomy wound never healed; reactivation of chest tuberculosis 7 yr. post- operatively; collapse of ver- tebral bodies T-6 and T-7 with recurrence of para- plegia; roentgenographic diagnosis: Pott's disease 7 yr. postoperatively
54 M 23	8 mo.	1 mo.	Normal	C-1 to C-6	Cervical adenitis and retropharyngeal mass incised and drained 6 mo. preoperatively; wound did not heal; guinea pig inocu- lation of mass positive for tuberculosis (reported after laminectomy)	Died 1st postoperative day; respiratory paralysis	Autopsy: epidural granula- tion tissue communicated with draining sinus of lateral neck; vertebral body C-2 carious

# A NEW TREATMENT FOR POSTOPERATIVE PULMONARY COLLAPSE

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Of all the complications following surgical procedures, those involving the lungs are among the most feared and the most commonly reported.<sup>1</sup> The incidence of atelectasis has been variously reported as causing from 3 to 70 per cent of all postoperative complications, with 40 per cent mortality among the persons affected.<sup>2</sup> In operations of the upper part of the abdomen the morbidity from respiratory complications is said to be about 10 per cent.<sup>2</sup> At the Kansas City Gen-

eral Hospital during two years in which careful records have been kept, the incidence of morbidity and mortality from respiratory complications is seen to be much lower (tables 1 and 2).<sup>2</sup> All patients with atelectasis and massive pulmonary collapse in this series recovered speedily. Pneumonia was named as the cause of death or was associated with other causes in 24 of 125 postoperative deaths. In most cases the pneumonia occurred as a terminal process a number of days following operation and was associated

TABLE 1.—Results in Cases in Which Anesthetic Was Used

	Number of Cases	Respiratory Complications, Number of Cases			Respiratory Complications, %	Mortality, Number of Cases			Respiratory Complications, %	Mortality, %
		Collapse	Atelectasis	Pneumonia		Collapse	Atelectasis	Pneumonia		
Spinal.....	718	2	7	14	3.1	0	0	0	0.28	1.8
Cyclopropane.....	816	0	2	13	1.6	0	0	1	0	0.27
Ether (open drop).....	275	2	3	5	3.2	0	0	1	0.73	1.8
Nitrous oxide-ether.....	19	1	0	10	57.9	0	0	2	5.2	52.6
Cyclopropane-ether.....	100	2	3	3	8.0	0	0	1	2.0	3
Nitrous oxide.....	136	0	0	3	2.3	0	0	2	0	2.3
Pentothal sodium.....	538	0	0	0	0	0	0	0	0	0
Spinal-gas.....	102	0	0	3	3.0	0	0	3	0	3.0
Total.....	2,704	6	15	51	2.6	0	0	24	0.22	1.8

To summarize this table, in 0.22 per cent of all cases in which an anesthetic was used there was massive collapse of the lungs; in 0.55 per cent atelectasis and in 1.8 per cent pneumonia, with an ultimate mortality of 0.88 per cent for all cases in which an anesthetic was used (33 per cent of the total morbidity from disease of the respiratory tract.)

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TABLE 2.—Percentage of All Cases Having Postoperative Complications

	Drop Ether, %	Cyclopropane, %	Spinal, %	Nitrous Oxide, %	Pentothal Sodium, %
Nausea and emesis.....	47	25	17	15	11
Distention.....	8	8	10.9	2	0
Catheterization and retention.....	21	14	15	18	4
Tachycardia.....	32	15	20.3	11	5.5
Pneumonia.....	1.5	1.7	2.0	2.0	0
Atelectasis.....	1.09	0.27	0.9	0	0
Massive collapse.....	0.73	0	0.28	0	0
Fall in blood pressure without shock.....	3.5	3.4	1.0	4.0	0
Shock.....	5.0	1.4	2.0	0	0
Headache.....	5.0	6.0	5.7	0	2.2
Other complications, as wound infection, neuritis, cough, irrational, embolism, etc.....	5.0	10.0	23.7	3	5.5

Read before the Kansas City Academy of Anesthesiology, Kansas City, Mo., May 2, 1945.

1. Adams, W. E.: Thoracic Surgery: Postoperative Pulmonary Atelectasis, *Am. J. Surg.* 56:180-191 (April) 1942.

2. Elkin, D. C.: Postoperative Pulmonary Complications, *Surg., Gynec. & Obst.* 70:491-493 (Feb.) 1940.

3. Grandstaff, E. H., and Schaeffer, W. C.: Progress in the Anesthetic Department of the Kansas City General Hospital, 1940, *J. Missouri M. A.* 38:352-353 (Oct.) 1941.

tive complications of all types,<sup>3</sup> the high percentage of oxygen which it is possible to give during the administration of the anesthetic and the lack of injury to the liver or kidneys or of other pathologic damage. Many of these patients



# RESECTION OF THE LUNG IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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BALTIMORE

Tuberculosis is a systemic infectious disease caused by a specific micro-organism. It most often involves the lung and is usually bilateral, but, fortunately, the major disease area is predominantly unilateral and often unilobar. Prevention of infection or establishment of acquired resistance<sup>1</sup> would be the ideal treatment. Progress is being made in both of these methods. Since prophylactic treatment is not entirely effective, early recognition of the disease is important. Great advances are being made in this direction by means of roentgenographic examinations of large groups of people.<sup>2</sup> Perhaps in the not too distant future every patient admitted to hospital will have a roentgenogram made of his chest, just as he now has a urinalysis and a biologic test for syphilis.

Chemotherapy would be the ideal method of treatment of the disease. Various chemical agents are being studied diligently for the arrest of pulmonary tuberculosis, but as yet an effective drug has not been found.<sup>3</sup>

The application of adequate medical measures supplemented by simple surgical procedures will prevent or cure early pulmonary tuberculosis in most cases. For valid reasons the disease will progress to a late stage in certain patients, and these cases must also be accepted for treatment.

Often in the later stages of the disease, irreversible structural changes occur in the bronchial system, thus causing the failure of simple therapeutic measures. It seems likely that effective chemotherapy, even though it could render the patient bacteriologically free of tubercle bacilli, would not relieve him of all symptoms.

Accurate diagnosis is extremely important in recognizing irreversible structural changes in the lungs and the bronchial system. The use of tomography, bronchography, determinations of intracavitary pressure, bronchoscopy, bronchospirometry and diagnostic pneumothorax as indicated will lead to the correct diagnosis of pulmonary lesions. Only with an accurate diagnosis can the outcome of surgical treatment be predicted. The finding of tubercle bacilli in the sputum has long been insufficient for diagnosis. The unexpected good result or the discouraging poor result from a surgical procedure usually is contingent on an incomplete diagnosis or a misunderstanding of the nature of the disease. Few phthisiologists would recommend thoracoplasty or pneumothorax in the presence of a known stenosis of a main bronchus. It is becoming more evident that the poor end results of thoracoplasty and pneumothorax often are caused by endobronchial disease.<sup>4</sup> Intracavitary drainage is indicated for a cavity with positive pressure but definitely contraindicated if there is an atmospheric or a negative pressure within the cavity.<sup>5</sup> In the present state of knowledge, thoracoplasty is contraindicated when a cavity is in a phase of increased pressure and should certainly not be recommended when pulmonary tuberculosis is complicated by bronchiectasis. Thoracoplasty is never justified as a trial method of treatment; however, a trial with pneumothorax often is permissible.

If the contralateral lung is free of disease, pulmonary resection appears to be the best treatment after the occurrence of irreparable damage, such as bronchial stenosis, bronchial disease with or without ulcerations not responding to bronchoscopic treatment, bronchiectasis and unsuccessful thoracoplasty. When such a condition exists, it is either because treatment failed in the early stages of the disease or because it was not started. The

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1. Rich, A. R.: *The Pathogenesis of Tuberculosis*, Springfield, Ill., Charles C Thomas, Publisher, 1944, 477.

2. Ashbury, H. E.; Whildin, J. G., and Rogers, T.: *Roentgenological Report of Chest Examinations*, N. J. Roentgenol. 48:347, 1942. Goorwitch, J.: *Mass Roentgenography and Admissions to Olive View Sanatorium*, Am. Rev. Tuberc. 50:214, 1944.

3. Pfuetze, K. H.: *Present Status of Chemotherapy of Tuberculosis from Clinical Standpoint*, Dis. of Chest 22:220, 1945.

4. Brantigan, O. C.; Hoffman, R., and Proctor, D. F.: *Endobronchial Tuberculosis*, Am. Rev. Tuberc. 45:477, 1942.

5. Vineberg, A. M., and Kunstler, W. E.: *The Determination and Treatment of Pressure Cavities in Pulmonary Tuberculosis*, Surg., Gynec. & Obst. 78:245, 1944.

mucus and obstruction; the high percentage of oxygen in this inspired closed ether atmosphere allows its almost immediate removal by the blood stream, leaving a collapsed lung behind one or numerous small obstructive masses of mucus.

Cyclopropane was followed by the fewest pulmonary complications as well as other types of complications, in spite of the fact that it is administered to those patients already extremely ill but requiring operation. It causes a negligible amount of bronchial irritation and production of mucus. In a few cases collapse follows administration of cyclopropane, particularly when combined with a large dose of morphine, because of the depression of the respiration from the removal of the carbon dioxide to produce purposely a shallow respiration and a quiet abdomen for surgical intervention.

Aspiration of blood or vomitus during or after operation is an important consideration also, as this may plug the bronchioles. If the airway does not seem to be perfectly clear at the end of operation, this aspiration should be done before the patient is removed to the ward.

The onset of pulmonary collapse occurs suddenly, usually during the first three days, with pain in the chest, dyspnea and a sharp rise in temperature and in pulse and respiration rates. The patient is usually found sitting up in bed, anxious, dyspneic and cyanotic. There is more or less fixation of the affected side, with dullness on percussion, absence of breath sounds, elevation of the diaphragm and shift of the area of cardiac dullness toward the affected side. The unaffected side is hyperresonant, and there are increased breath sounds.<sup>12</sup> The sputum is scanty at first but quickly becomes abundant and mucopurulent. The white blood cell count may be 15,000 to 20,000. The roentgenogram is characteristic, with elevation of the diaphragm on the affected side, narrowing of the intercostal spaces and deviation of the heart and other mediastinal structures to the affected side, the lung appearing dense and homogenous.

Treatment of such collapse is, of course, primarily prophylactic. As soon as the operative schedule is posted for the following day, the intern on the anesthesia service and I examine each patient and plan the type of anesthetic which will be the best, considering the pathologic condition of the patient, the type of operation proposed and the use of cautery or roentgen ray equipment. A member of the anesthesia department then writes orders for the preoperative medication, giving a small dose of morphine for all patients except those who are young and vigorous. By small dose is meant  $\frac{1}{16}$  grain

(0.0037 Gm.) to  $\frac{1}{8}$  grain (0.007 Gm.) for those above 50 years,  $\frac{1}{8}$  grain to  $\frac{1}{6}$  grain (0.01 Gm.) for those from 50 to about 25 years and  $\frac{1}{8}$  grain for those in good condition, in their twenties and thirties. Occasionally  $\frac{1}{4}$  grain (0.015 Gm.) is given in this group. Scopolamine is given in combination with the morphine preceding spinal anesthesia for further sedation,  $\frac{1}{150}$  grain (0.0004 Gm.) to  $\frac{1}{300}$  grain (0.0002 Gm.) being given with increasing age. Atropine is given preceding an anesthetic administered intravenously, as it has been found that there is more likely to be a fall in blood pressure during the administration of pentothal sodium if it has been preceded by the use of scopolamine. Atropine is also given to young children in preference to scopolamine, which rather seriously depresses them. Administration of the anesthetic is refused until the patient has received atropine or scopolamine for the proper interval previous to operation. Barbiturates are given to all patients preceding use of caudal, epidural or spinal anesthesia to avoid procaine reactions through depression of the central nervous system from stimulation of procaine and its derivatives. Barbiturates are given to those patients to receive nitrous oxide anesthesia to depress the metabolism further, which is necessary when administering this weak gas. They are also given preceding use of cyclopropane to decrease vagal tone and prevent cardiac arrhythmia from the combination of morphine and cyclopropane.<sup>7</sup> Ortol sodium is given to older people, over 50, and pentobarbital sodium in one or two 1.5 grain (0.009 Gm.) doses to younger patients. Seconal when combined with even a small dose of scopolamine has been found to be too depressing to the respirations of old people. Morphine and barbiturates are not given preceding tribromoethanol, as this combination produces severe respiratory depression. At the close of the anesthesia, an attempt is made to have the patient partially awake and to have his pharyngeal reflex back. Nitrous oxide is given during the last few minutes of cyclopropane anesthesia in order to fill the lungs with a substance which is much more slowly absorbed in case a portion of the lung should be cut off behind a mucus plug. Nitrous oxide requires several hours to be dissolved by the blood stream, while cyclopropane and oxygen are removed in a few minutes and in that case would leave a portion of lung collapsed in a short time. I have not seen a case of atelectasis develop after this

7. Robbins, B. H.; Baxter, J. H., and Fitzhugh, O. G.: The Use of Barbiturates in Preventing Cardiac Irregularities Under Cyclopropane or Morphine and Cyclopropane Anesthesia, *Ann. Surg.* **110**:84-93 (July) 1939.

type of tuberculous pulmonary disease for treatment by lobectomy.

CASE 9.—V. G. was a white woman aged 29 years, whose present condition started with pleurisy in 1936. An acute illness in 1938 was diagnosed as tuberculosis. On Oct. 26, 1942 a temporary paralysis of the phrenic nerve was produced for a small apical cavity. The patient was kept at rest in bed, and a roentgenogram showed that the cavity had disappeared entirely; the sputum also gave a negative reaction. Contrary to medical advice, she became pregnant and delivered a normal baby. This was followed by a second temporary paralysis of the phrenic nerve on Nov. 22, 1944. In spite of treatment, there was extension of the apical disease and an opening of the apical cavity. The sputum was positive for tubercle bacilli. Pneumothorax could not be initiated. A thoracoplasty was advised but refused. The parents of the patient also opposed a thoracoplasty and elected lobectomy, and this decision was acceptable to the physicians.

On May 4, 1945 a lobectomy of the upper lobe of the right lung was performed. The pleural space was liberated completely by adhesion of the parietal and visceral pleurae. The lung was easily freed from the parietal pleura, except over the cavity, and that area was freed from the chest wall by extrapleural stripping. The pleural cavity was closed without drainage. The patient's postoperative course was entirely uneventful.

*Comment.*—This is the only elective lobectomy and the only lobectomy of an upper lobe in this series. The patient was an excellent candidate for thoracoplasty. As usual, the sputum was negative for tubercle bacilli immediately after the operation. It is the only instance of a lobectomy that was closed without drainage. Aspiration of the chest was not necessary. Time alone will determine the future course of tuberculosis in this patient.

#### COMMENT

Dissection of the hilar structures, permitting individual ligation of the pulmonary artery and vein and allowing adequate suture of the bronchus with silk, has greatly reduced the development of bronchial fistulas. None has occurred in this small series. In the earlier cases the bronchial division was made immediately distal to the point of division of the secondary bronchus from the major bronchus to the lobe.<sup>9</sup> This technique caused a long bronchial stump, but bronchial closure was made at a narrow point. The recurrence of tuberculosis of the bronchial stump led to a change of technic for the last patient, in whom division of the bronchus was made at the point at which the bronchus to the lobe branched from the main bronchus; thus, a short bronchial stump was obtained.

Hilar dissection in persons with tuberculosis has been uniformly easier than in persons

with other pulmonary conditions requiring a lobectomy or pneumonectomy. Interlobar fissures usually are incomplete; therefore pneumonectomy is a cleaner operation because pulmonary tissue invariably must be cut through in a lobectomy. There is almost invariably an incomplete fissure between the upper and lower lobes posteriorly. This incomplete interlobar fissure is a particularly well known anatomic fact. Unfortunately, tuberculous disease often is located in the upper portion of the lower lobe, which places it at the region of the incomplete fissure. Every effort is made to avoid cutting into tuberculous tissue; thus, resection frequently must be carried into the remaining healthy lobe. Technically, it is often less difficult to do a pneumonectomy.

No drainage is used in cases of pneumonectomy and lobectomy of the upper lobe, since there is no method of immediately obliterating the pleural space. Two grams of sulfanilamide and 150 to 200 cc. of chloroazodin (1:3,300) in sodium tetradecyl sulfate (1:500) are placed in the pleural cavity. There is experimental evidence<sup>10</sup> that this combination of drugs has great bactericidal effect, and the clinical application has been satisfactory.<sup>11</sup> The same drug and solution are placed in the pleural cavity when a lobectomy of the lower lobe is done, even though it is drained. If the remaining lobes are freed completely from the parietal pleura, the pleural space can be obliterated quickly by using a low negative pressure suction apparatus.<sup>9</sup> Obliteration of the pleural space usually will prevent both pyogenic and tuberculous infections. It also offers some assurance against opening of the bronchial stump. All lobectomies of the lower lobes in this series were drained by negative suction. Since penicillin now is available, it is used by intramuscular injection before and after operation.

From an empiric study of many cases of thoracoplasty it appears that the preoperative and postoperative administration of a sulfon-

10. Neter, E.: An in Vitro Study on the Synergistic Action of Sulfamido Compounds and Azochloramid upon Various Pathogenic Microorganisms, *J. Pharmacol. & Exper. Therap.* 74:52, 1942. Petroff, S. A., and Schain, P.: The Enhancement of Bactericidal Properties of Well Known Antiseptics by Addition of Detergents, *Quart. Bull., Sea View Hosp.* 5:372, 1940. Schmelkes, F. C., and Wyss, O.: Inactivation of Sulfonamide Inhibitor by Azochloramid, *Proc. Soc. Exper. Biol. & Med.* 49:263, 1942.

11. Brantigan, O. C., and Owings, J. C.: Sodium Tetradecyl Sulfate Used in the Treatment of Acute Pyogenic Empyema of the Pleural Cavity, *Bull. School Med. Univ. Maryland* 26:247, 1942. Brantigan and Looper.<sup>9</sup>

Brantigan, O. C., and Looper, E. A.: The Medical and Surgical Treatment of Lung Abscess, *Ann. M. J.* 37:199, 1944.

nea and expectorating gray sputum. Some distention was present. Her temperature was 102.2 F. Codeine was given for relief of pain. November 3 the chest was examined roentgenologically, and the condition of the patient was reported to the anesthesia department. She was found dyspneic and anxious and cyanotic and she was coughing and retching almost continuously. The temperature was 102.2 F. and the pulse rate 120. Roentgen ray examination showed diffuse clouding of the entire left lung, and the central shadows were displaced toward this side, with increased aeration on the right. Cocainization of the larynx was done, with expectoration in a few minutes of a large mucus plug and large amounts of purulent mucus. A roentgenogram taken at once showed partial clearing of the left pulmonary field with progressive clearing November 4 and 5. Inhalations of carbon dioxide and oxygen were started and also chemotherapy with sulfathiazole; blowing up of blow bottles was instituted, with relief of the collapse, though a pulmonic process in the base of the left lung persisted until November 17.

This case illustrates the necessity for recognition and treatment of a condition of collapse at once before pneumonia begins, which happens speedily in a congested and airless area of lung and which prolongs the recovery period a number of days.

CASE 2.—E. D., a poorly nourished white man 48 years old, was brought to surgery on July 15 for repair of a recurrent inguinal hernia on the left side, which had been repaired eight years ago. His history was noncontributory except for the fact that he smoked excessively and had a chronic nonproductive cough. Physical examination revealed carious teeth with spongy, receding gums and a moderately injected pharynx. A few moist rales were heard in the left axilla. Twelve milligrams of pontocaine hydrochloride solution was given in the second lumbar space; the hernia was repaired without incident in fifty-five minutes, and the patient was returned to the ward in good condition. Inhalations of carbon dioxide and oxygen were refused, and the patient refused to take deep breaths or to cough. A roentgenogram was taken July 16 on account of pleuritic pain in the right base of the chest, with a friction rub; it revealed clouding of the base of the right lung with elevation of the diaphragm, and was interpreted by the roentgen ray department as "suggestive of pleurisy." The temperature at this time was 99.8 F. Morphine sulfate,  $\frac{1}{2}$  grain [0.01 Gm.], was being given three times a day. His temperature rose to 102.6 F. on July 17, and he had severe pain in the back. Administration of sulfathiazole was begun, with rapid improvement. The temperature was 99 F. On July 19 another roentgenogram was taken on account of increased pain, which revealed a large shadow above the right side of the diaphragm with a shift of the trachea to the right. The throat was cocainized with 10 per cent cocaine solution, and the patient coughed up a large mucus plug and stated that the pain was less intense. He remained comfortable, and his condition steadily improved. Use of sulfathiazole together with ammonium sulfate was continued for forty-eight hours with no further incident.

CASE 3.—N. G., a poorly nourished woman 27 years old, was brought to surgery on June 19 for suspension and perineorrhaphy. The history revealed chronic pelvic inflammatory disease, with recent septic abortion with hemorrhage. The hemoglobin content was 81 per cent, the sugar content 104 mg., the nonprotein nitrogen level

27.9 mg. and the creatinine content 1.4 mg. per hundred cubic centimeters. The operation preceding this one had been canceled, and so the patient was brought to the operating room and premedication of secenal, 3 grains (0.19 Gm.), given at 7:30 a. m., morphine sulfate  $\frac{1}{6}$  grain (0.01 Gm.), and scopolamine hydrobromide  $\frac{1}{200}$  grain (0.0003 Gm.), being given at the same time. Administration of cyclopropane was begun at 7:42 a. m., followed by closed ether. The surgeon had insisted that the anesthetic be begun immediately, stating that it made no difference when the premedication was given. A dilation and curettage, perineorrhaphy, trachelorrhaphy and Gilliam's suspension were done during the next hour and thirty minutes, and the patient was returned to the ward in good condition at 9:50 a. m. At 10:30 a. m. on June 20 she was seized with sudden pain in the right side of the chest, with dyspnea, anxiety and tachycardia. Examination revealed the right side of the chest unexpansive on respiration, an absence of breath sounds in the right base and coarse rales heard in the right apex. Roentgen ray examination showed massive collapse of the right lung, with the mediastinum and trachea shifted to the right. Cocainization of the throat was done within half an hour and coughing encouraged. A large hard mucus plug was expectorated, with the patient experiencing great relief of dyspnea and anxiety. The cyanosis improved almost at once. Roentgen ray examination showed partial clearing of the chest. Inhalations of carbon dioxide and oxygen and blowing up of blow bottles were started. By 4 p. m. the roentgenogram revealed the right side of the chest nearly clear, with the diaphragm returned to a normal level. Sulfathiazole was discontinued June 21, and the patient remained free from further symptoms.

CASE 4.—R. O., a poorly nourished woman 43 years old, was brought to surgery March 18 for exploratory laparotomy on account of large pelvic masses. She had been bleeding profusely for four months, with a hemoglobin content on her admission to the hospital (February 26) of 27 per cent. The rest of the history was noncontributory, and physical examination at this time revealed exceedingly carious teeth and spongy gums and a soft blowing mitral systolic murmur disappearing on exercise. Hemoglobin content at the time of operation was 65 per cent, the sugar content 108 mg., the nonprotein nitrogen level 31.6 mg. and the creatinine level 1.7 mg. per hundred cubic centimeters. The urine test revealed nothing abnormal. Premedication of morphine,  $\frac{1}{6}$  grain (0.01 Gm.), and scopolamine hydrobromide,  $\frac{1}{200}$  grain (0.0003 Gm.), was given and fifty-five minutes later drop ether was begun, as the surgeon insisted that ether be used for all of his patients. Bilateral salpingo-oophorectomy was done during a one hour operation without incident, and the patient was returned to the ward in good condition at 10:30 a. m. Her condition remained good until March 19 at 8 p. m., when she complained of shortness of breath and pain in the right side of the chest. The temperature was 102.8 F. and the pulse rate 160. There was an absence of breath sounds in the right side and hyperresonance in the left side of the chest. The medical service was consulted and gave advice to treat the patient as for pneumonia. Administration of sulfapyridine was started, but by morning the patient was worse and symptoms were more pronounced. A roentgenogram taken during the morning revealed a complete collapse of the right side of the chest (fig. 1 A). At 2:15 p. m. the anesthesia department was consulted, and the throat was cocainized at once with 10 per cent cocaine. During the procedure the patient was thrown into a paroxysm of coughing that resulted in the expectoration of copious quantities

method. Martin, Field and Hall<sup>8</sup> (1932) described a method for obtaining isometric contraction of muscles in situ, but the animal was killed with the experiment. Eccles<sup>9</sup> (1941), in a carefully controlled set of experiments on cats, recorded muscle contraction by means of an isometric mirror myograph, but in his experiments, again, it was necessary to kill the animal after one stimulation. The only studies of muscle contraction in the same animal over a period of time were made by Hartman and Blatz<sup>10</sup> (1920). On anesthetized rabbits, which were strapped to a board, had sandals tied to their feet in such a manner that contraction of the gastrocnemius group of muscles caused them to lift a weight. Stimulation was supplied through a salt pad over the sciatic region and a brass electrode applied to the muscle group.

In our problem the datum most significant clinically was the power of the muscles. Changes in power of a muscle can be followed only by use of the same animal, and from the review it is apparent that no satisfactory method had been developed for stimulating and recording muscle function repeatedly in the same animal. For this reason we attempted to design a method of study of muscle power which could be used repeatedly and which, in order that the data obtained would have the greatest clinical significance, best simulated clinical conditions with the sacrifice of physiologic accuracy.

We were immediately faced with the question, what is the measure of the power of a muscle? Is the ultimate force that the muscle can exert after subjected to progressively stronger re-

peated or sustained galvanic or faradic stimulation. Such experiments damage the muscle, and the results are variable. Likewise, experiments on fatigue and on the ability of a muscle to lift a given weight at a variable height were of little value. It was noted that when the strength of the faradic current is increased gradually, a point is reached at which the twitch of the muscle caused by the completion of the circuit is followed by a break in the circuit. This break value forms a plateau which is maintained over a range of several amperes and is constant for the same normal muscle.

Martin, E. G.; Field, J., and Hall, V. E.: A Method for Obtaining and Recording Isometric Contractions of Mammalian Skeletal Muscle in Situ, *Am. J. Physiol.* 102:476-480, 1932.

Eccles, J. C.: Disuse Atrophy of Skeletal Muscle, *Proc. Roy. Soc. (London)* 2:160-164, 1941.

Hartman, F. A., and Blatz, W. E.: Studies in the Denervation of Mammalian Muscle: III. The Effect of Denervation on the Response to Massage and Electrical Stimulation, *J. Physiol.* 45:1-20, 1920.

when the experiment is repeated at weekly intervals. We have used the power exerted by a single twitch of the muscle when stimulated at the plateau level as a measure of the power of the muscle. In some of our cats the gastrocnemius-soleus group of muscles of each leg exerted a force of over 20 pounds (9.1 Kg.) in a single twitch.

#### METHOD

Briefly, the method consists in stimulating the gastrocnemius group of muscles in a cat and recording the contraction by means of a torsion lever and kymograph (fig. 1). The cat is deeply anesthetized, sodium pentobarbital being used in a dose of 0.6 cc. per kilogram of body weight, intraperitoneally, and the hind-legs are clipped free of long hair and prepared with cetylpyridinium chloride and alcohol. After this, the

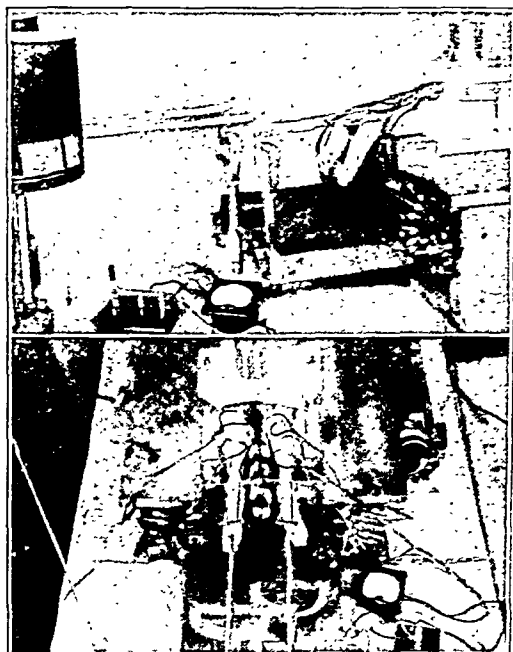


Fig. 1.—Two views of an anesthetized cat in the apparatus.

The cat is mounted on the stimulating table by means of three clamps, one at each ankle and one across the pelvis and thighs.

These clamps are fastened to the same block of wood, the clamp block, which is, in turn, attached to the stimulating table. Each ankle clamp consists of a U-shaped piece of brass which, through slots, can be adjusted to various heights on the clamp block, depending on the size of the cat. Projecting centrally about  $\frac{3}{8}$  inch (1 cm.) from one arm of the U is a  $\frac{1}{8}$  inch (0.3 cm.) metal rod pointed at the end. A similar rod is screwed through the other arm of the U and is made adjustable by a thumbscrew at its end. The pelvic clamp is a plaster of paris impression of the pelvis and upper parts of the thighs of the animal, made in two pieces. One piece is a mold of the ventral side and the other a mold of the dorsal side of the animal. Each of these casts fits on two upright bolts fastened to the clamp block and can be tightened firmly around

at 10:30 a. m., followed by closed ether anesthesia for maintenance. Lysis of extensive adhesions of the omentum into the pelvis was done. The operation lasted an hour and fifty-three minutes, and the patient was returned to the ward in good condition at 12:50 p. m.

sulfate and sulfapyridine. Copious expectoration resulted from cocaineization of the throat, with pronounced relief experienced by the patient. A roentgen ray examination at 8 a. m. revealed two-thirds clearing of the left base, with still a slight shift of the mediastinal

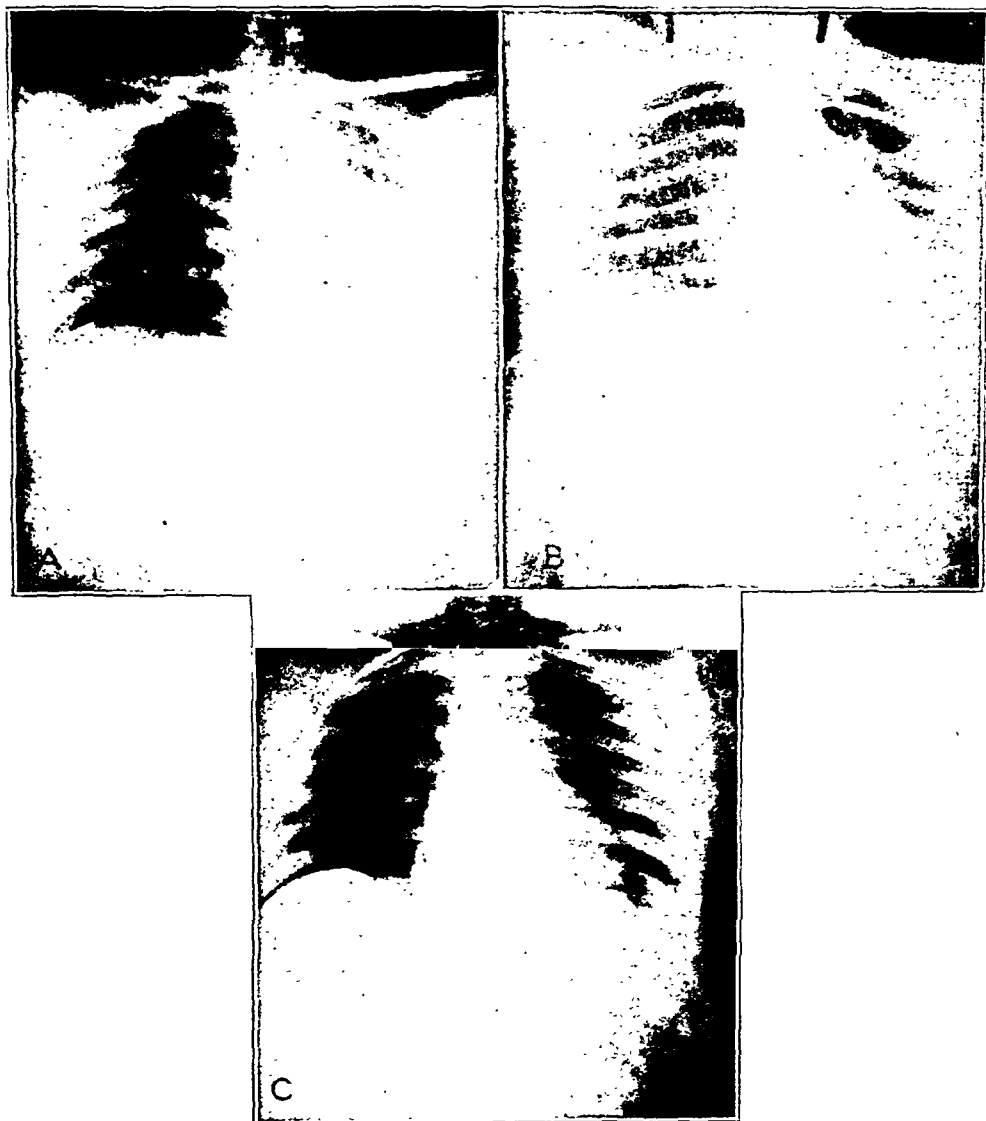


Fig. 2 (case 5).—*A*, showing collapse of the lower lobe of the left lung before treatment. *B*, showing reexpansion of the left base shortly after treatment and two hours after initial collapse. *C*, showing complete reexpansion and clearing of the left lung ten hours after initial collapse, with immediate treatment.

She was talking at 1:50 p. m. At 6 a. m. January 23, she was found cyanotic and complaining of pain in the chest. A roentgenogram revealed collapse of the left lung (fig. 2*A*). Swabbing of the throat with epinephrine and cocaine was started, with inhalations of carbon dioxide and oxygen and use of ammonium

shadow (fig. 2*B*). Roentgen ray examination at 4 p. m. showed complete clearing of the base of the left lung (fig. 2*C*).

This case also illustrates the value of immediate treatment in preventing pneumonia following collapse of the lung.

TABLE 2.—*Muscle Strength in Disuse Atrophy Cats Following Removal of Cast (Second Study)*

Immobilized leg is listed first; control leg, second.

	Cat	Leg	Mean Normal, %	Maximum Deviation from Mean Normal, %	First Week After Cast Removed, %	Second Week After Cast Removed, %	Third Week After Cast Removed, %	Fourth Week After Cast Removed, %	Sixth Week After Cast Removed, %	Eighth Week After Cast Removed, %	Ninth Week After Cast Removed, %
Relaxed	55	R	32.1	6.9	29.0	33.0	35.0	35.0	32.0	Died	
		L	23.5	9.5	37.5	32.5	39.5	33.0	33.0	Died	
	59	L	35.8	1.7	35.0	34.0	36.0	41.0	33.5	34.5	
		R	34.5	5.5	37.5	39.5	33.5	41.5	34.0	33.5	
	69	R	33.3	0.6	29.0	32.0	34.0	32.0	31.5	34.0	
		L	30.7	4.0	26.5	37.5	36.0	35.0	33.5	40.5	
	72	L	41.1	5.1	45.0	35.5	45.5	39.0	40.5	36.5	
		R	38.5	7.0	52.5	45.0	43.0	46.0	26.5	42.5	
	73	L	29.3	3.1	26.5	26.5	29.0	31.5	28.5	27.5	
		R	30.0	4.3	33.0	32.5	34.0	35.5	27.5	30.5	
	76	R	28.1	2.5	29.5	30.5	40.5	35.0	34.5	Died	
		L	33.0	6.1	39.0	36.5	40.0	43.5	38.0	Died	
	77	R	30.0	0.0	16.5	20.5	27.5	27.0	26.5	24.5	
		L	26.2	12.2	26.5	31.5	36.5	35.0	30.0	26.0	
	82	R	33.0	5.2	26.0	30.5	34.0	32.0	32.0	Died	
		L	36.5	8.2	38.0	37.0	41.5	39.0	36.0	Died	
Stretched	62	L	35.1	2.2	24.5	29.5	27.0	28.0	Died		
		R	31.5	5.0	41.5	41.5	37.5	32.0	Died		
	74	R	34.7	7.8	32.0	36.0	37.5	32.0	27.0	27.5	
		L	32.2	7.1	28.0	35.0	31.5	35.0	34.5	31.5	
	75	R	33.7	1.8	29.5	35.0	35.0	33.5	18.5	23.0	
		L	33.3	5.7	32.0	40.0	32.0	36.5	32.0	34.5	
	78	L	35.5	0.0	25.5	27.5	25.0	25.0	26.5	29.0	
		R	39.2	8.4	40.5	41.5	40.5	44.0	45.0	40.0	
	83	R	44.8	4.9	27.5	33.0	22.0	25.5	32.0	29.0	
		L	29.5	6.8	40.5	36.0	35.0	39.5	34.0	30.5	
Neutral	54	R	37.6	2.9	34.0	37.0	35.0	27.0	27.0	....	27.5
		L	36.5	6.8	33.0	36.5	32.5	25.0	34.0	....	26.5
	56	R	37.8	3.4	26.0	31.0	28.5	32.0	30.0	....	32.5
		L	34.8	5.2	39.0	38.5	38.0	37.5	33.5	....	42.5
	84	L	31.3	2.2	41.0	46.5	26.5	26.0	33.0	....	33.5
		R	32.2	11.5	46.0	47.5	41.5	35.0	39.5	....	33.5
	87	R	28.5	5.3	29.0	33.0	30.0	Died			
		L	27.3	8.1	28.5	32.0	27.5	Died			
	88	L	39.5	7.6	42.5	45.5	41.0	41.5	42.5	....	30.0
		R	43.5	11.5	47.5	48.0	49.0	50.0	44.0	....	26.0

TABLE 3.—*Significant Variation of Muscle Strength from the Mean Normal Following Cast Removal in Disuse Atrophy Cats (Second Study)*

	Cat	Mean Normal Twitch Strength of Immobilized Leg	Maximum Deviation from Mean Normal, %	Actual Maximum Deviation from Mean Normal	Variation in Excess of Maximum Deviation						
					First Week After Cast Removed, %	Second Week After Cast Removed, %	Third Week After Cast Removed, %	Fourth Week After Cast Removed, %	Sixth Week After Cast Removed, %	Eighth Week After Cast Removed, %	Ninth Week After Cast Removed, %
Relaxed	55	32.1	6.9	2.2	-2.8	.....	+ 2.2	+ 2.2	.....	Died	
	59	35.8	1.7	0.6	- 0.6	- 3.4	.....	+12.8	- 7.5	- 1.2	
	69	33.3	0.6	0.2	-12.4	- 3.3	+ 1.5	- 3.3	- 4.8	+ 1.5	
	72	41.1	5.1	2.1	+ 4.4	- 8.5	+ 5.6	.....	.....	- 6.1	
	73	29.3	3.1	0.9	- 6.5	- 6.5	.....	+ 4.4	.....	- 3.1	
	76	28.1	2.5	0.7	+ 2.5	+ 6.0	+41.6	+22.0	+20.3	Died	
	77	30.0	0.0	0.0	-45.0	-31.6	- 8.3	-10.0	-11.7	-15.3	
	82	33.0	5.2	1.7	-16.1	- 2.4	.....	.....	.....	Died	
				Average	- 9.6	- 6.2	+ 5.3	+ 3.5	- 0.5	- 5.4	
Stretched	62	35.1	2.2	0.8	-28.9	-13.7	-20.8	-18.0	Died		
	74	34.7	4.9	1.7	- 2.9	.....	+ 3.2	- 2.9	-17.3	-15.9	
	75	33.7	1.8	0.6	-10.7	+ 2.1	+ 2.1	.....	-43.2	-30.0	
	78	35.5	0.0	0.0	-28.2	-22.6	-29.6	-29.6	-25.3	-18.3	
	83	44.8	3.1	1.4	-35.5	-23.2	-25.4	-17.6	-25.4	-32.2	
				Average	-21.1	-11.5	-14.1	-13.6	-27.5	-24.1	
Neutral	54	37.6	2.9	1.1	- 6.6	.....	- 4.0	-23.3	-25.3		-23.9
	56	37.8	3.4	1.3	-27.8	-14.6	-21.2	-11.9	-17.2		-10.6
	84	31.3	2.2	0.7	+28.8	+46.4	+14.4	+12.5	+ 3.2		+ 4.8
	87	28.5	5.3	1.6	.....	+10.5	.....	Died			
	88	39.5	7.6	3.0	.....	+ 7.6	.....	.....	.....		-16.5
				Average	- 1.1	+10.0	- 2.2	- 6.1	- 9.8		-11.5

..... Indicates variation not in excess of actual maximum deviation.

5 per cent of body weight, a value in agreement with that originally found by Blalock, Harkins and others<sup>1</sup> (chart 1).

Along with the local accumulation of fluid, sodium enters the injured area; this amounts to 0.10 milliequivalent for a 15 Gm. mouse and is greater by 0.03 milliequivalent than the amount which can be accounted for by the local increase in fluid. This local increase in sodium is equivalent to the entire sodium in the circulating blood or one fourth of that in the total extracellular fluid. This rapid accumulation of fluid and sodium occurs at the expense of the uninjured tissues, which are correspondingly dehydrated.

During the same two hour period, the injured area loses approximately one third of its total potassium, amounting to 0.03 milliequivalent per 15 Gm. mouse (chart 1). This quantity of potassium is thus released from the traumatized area into the rest of the body; its significance will be discussed later. It is of interest that the potassium loss from the injured area corresponds approximately to the sodium gain, which is in excess of that calculated to enter with the edema fluid, suggesting that an exchange of potassium

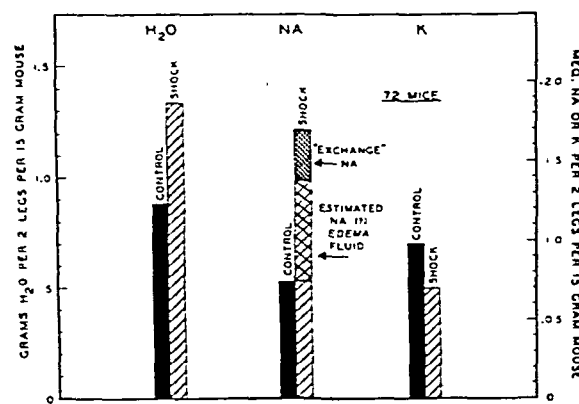


Chart 1.—Changes in water, sodium and potassium in the hindlegs of mice subjected to tourniquets for two hours. Analyses two hours after removal of tourniquets. Values represent the total amounts in the two legs of a 15 Gm. mouse. Control values from normal mice studied simultaneously.

for sodium takes place in injured tissues; evidence that this can occur in vitro has been presented by Eichelberger and Hastings<sup>6</sup> and that it can occur in vivo by Manery and Solandt.<sup>7</sup>

6. Hastings, A. B., and Eichelberger, L.: The Exchange of Salt and Water Between Muscle and Blood: I. The Effect of an Increase in Total Body Water Produced by the Intravenous Injection of Isotonic Salt Solutions, *J. Biol. Chem.* **117**:73-93 (Jan.) 1937.

7. Manery, J., and Solandt, D.: Studies in Experimental Traumatic Shock with Particular Reference to Plasma Potassium Changes, *Am. J. Physiol.* **138**:499-511 (Feb.) 1943.

The magnitude of these local changes in fluid and electrolyte have also been studied by Fox and Keston<sup>8</sup> with the use of radioactive sodium, and our results are substantially in agreement.

#### URINARY STUDIES

In addition to local alterations in the injured area, some estimate of the electrolyte changes

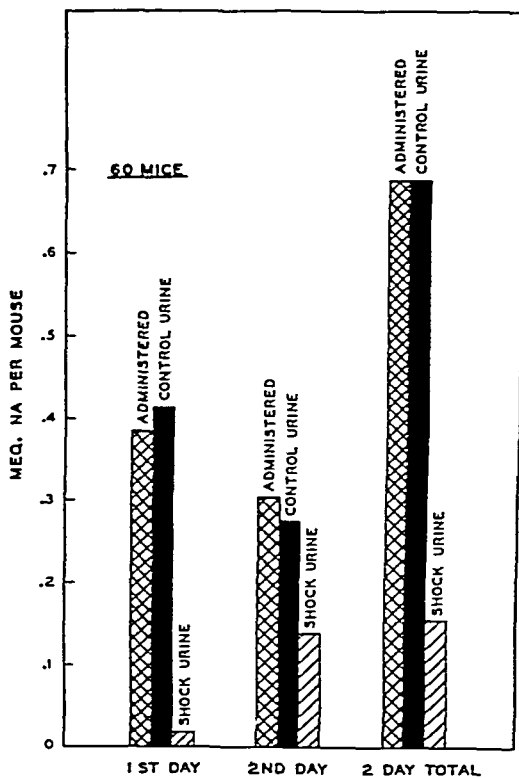


Chart 2.—Sodium excretion in urine of normal and shocked (tourniquet) mice. Both groups received 0.385 milliequivalent of sodium orally the first day and 0.302 milliequivalent the second day. Practically complete retention the first day and 72 per cent retained in forty-eight hours. Nine-tenths per cent solution of sodium chloride was administered.

that are occurring in the rest of the body and of fluid and electrolyte needs in shock may be obtained by urinary studies. Mice in which death from shock was prevented by therapy with 0.9 per cent solution of sodium chloride were placed in metabolism cages for quantitative collection of urine. Normal animals similarly treated with sodium chloride served as a basis for comparison.

The quantity of sodium retained by the shocked animal after administration of isotonic solution of sodium chloride may serve as some index of

8. Fox, C. L., Jr., and Keston, A. S.: The Mechanism of Shock from Burns and Trauma Traced with Radium, *Surg., Gynec. & Obst.* **80**:561-567 (June) 1945.



be done with relative safety. We further believe that when practical internal fixation should be used for fractures complicated by nerve lesions in order that external fixation may be reduced to a minimum. For this, there may be a place for the dual plates recently described by one of us (J. A. K.).

During the course of the work, we have thought of several means to improve the method and to eliminate obstacles which were encountered. Since we cannot effect them at this time, we make them as suggestions to any one interested in carrying this work further.

1. In denervated muscle, a satisfactory plateau could probably be obtained on stimulation if smaller experimental animals were used. The main factor in our inability to obtain this plateau was the size of the muscle which was so great in cats that stimulation of all the muscle fibers required current strengths which stimulated the fibers nearest the electrodes more than once. The smaller the muscle mass, the less important this factor would be.

2. Arcing across the points of the hand switch was another difficulty. A thyrotron would eliminate this, give better control of stimulating currents and make possible their use at much higher values acting for a shorter time. It could also be set to deliver a standard number of stimuli at each current strength used, thus eliminating excess stimulation and any fatigue factor which that may introduce.

3. The twitch measures immediate power but gives no indication of endurance. A study of tetanic strength in disuse and denervation atrophy may yield important information. Such a study was not possible with our apparatus because the inductorium could not carry the necessary current strength. A thyrotron, however, would provide a means for constant strength tetanic stimulation at high currents.

#### SUMMARY

This study attempts to determine two things: (1) the optimum position of fixation of limbs in order to conserve muscle power and (2) the

best method of treatment of muscles paralyzed by loss of nerve supply.

A review of the literature on muscle physiology shows that in most of the studies of disuse and denervation atrophy weight has been used as a criterion of the atrophy. Functional studies have employed methods requiring the killing of the animal after one stimulation. Only one functional study has been reported in which the same animal was repeatedly stimulated, and this method was not satisfactory for our purpose.

A method was developed for recording the twitch strength of the gastrocnemius-soleus group of muscles in cats. By means of the described method, animals have been stimulated as much as twelve different times without noticeable ill effect.

In a series of 51 normal cats stimulated at weekly intervals, this method yielded normal values for one leg, which showed only 4.6 per cent average maximum deviation from the mean, with a maximum deviation range of 0 to 8.3 per cent.

This method was applied to the study of disuse atrophy. After normal values were determined legs were immobilized for six weeks, with the muscle group in stretched, relaxed and neutral positions. Stimulation for eight weeks following removal of the cast showed moderate and persistent disuse atrophy in the muscles which were stretched, whereas the relaxed and neutral groups showed little consistent effect.

Denervated cats also were immobilized in various positions, but the study was unsatisfactory because no definite contraction plateau could be obtained in response to stimulation.

On the basis of the data obtained from denervated cats, however, the suggestion is made that denervated muscles atrophy less if left alone than if immobilized. Emphasis is also placed on repairing the nerve before the bone is healed when fractures are complicated by peripheral nerve injuries.

Dr. George Bishop, Professor of Biophysics, Washington University School of Medicine, has given help, without which this method could not have been developed.

Clarence E. Rupe, M.D., has given technical assistance in some of these experiments.

a basis of various experimental evidence, potassium has been suggested in this role.<sup>11</sup> While some recent evidence supports this view,<sup>12</sup> the importance of potassium has not been generally accepted. This is due in part to the fact that previous studies have been confined to changes in the blood or isolated tissues, and consequently quantitative data on the magnitude of the total changes were not available and also because the observed alterations were interpreted in terms of the normal rather than the shocked animal.

The following observations have been made<sup>5</sup> in an attempt to evaluate the significance of the potassium release in traumatic shock:

(a) In a shocked animal the toxicity of administered potassium increases six to nine times above that for a normal animal (chart 3). This is not the result of a general increase in susceptibility to toxic agents, for under similar conditions the toxicity of magnesium and quinidine (used as drug controls) was less than doubled.

(b) The amount of potassium released in shock, as indicated by analyses of the entire injured area and by urinary studies, is toxic for a normal animal when given intravenously or intraperitoneally and for an anuric (nephrectomized) animal when given subcutaneously and is several times the fatal dose for a shocked animal when given by any route (chart 3).

(c) The elevation of serum potassium in the shocked animal cannot be interpreted in terms of the elevation required to kill a normal animal. Rabbits in shock that are killed by injections of potassium chloride show terminal serum potassium levels (13.20 milliequivalent per liter, with a standard error of 0.22) within the same range as those found in shocked rabbits without treatment with potassium chloride that die from shock several hours later (12.08 milliequivalent with a standard error of 0.35). These values are lower than those obtained for normal rabbits that are killed by injections of potassium chloride (16.58 milliequivalent with a standard error of 0.68). These results suggest that the moderate elevations of serum potassium seen in shock may have greater significance than is usually attrib-

uted to them, particularly in relation to the terminal phases of this condition.

Not only is the shocked animal abnormally sensitive to administered potassium. It is possible to produce withdrawal of fluid and sodium from the body by the intraperitoneal injection of dextrose solutions.<sup>13</sup> By the use of this technic, it has been demonstrated that the shocked animal is also highly susceptible to any additional loss of fluid or sodium.<sup>5</sup>

The evidence indicates that these three factors, fluid loss, sodium loss and potassium toxicity, are interdependent. While in shock the magnitude of each change may not in itself be sufficient to produce death, their combined effects augment one another and may have an important influence on mortality in shock.

There are various types and various degrees of shock, in which a variety of other biochemical changes have been shown to exist<sup>14</sup>; like-

13. Schechter, A. J.: Electrolyte and Volume Changes in Fluids Injected into the Peritoneal Cavity, *Yale J. Biol. & Med.* **4**:167-185 (Dec.) 1931. Darrow, D. C., and Yan-net, H.: Changes in Distribution of Body Water Accompanying Increase and Decrease in Extracellular Electrolyte, *J. Clin. Investigation* **14**:266-275 (March) 1935; Metabolic Studies of Changes in Body Electrolyte and Distribution of Body Water Induced Experimentally by Deficit of Extracellular Electrolyte, *ibid.* **15**:419-427 (July) 1936.

14. (a) Russell, J. A.; Long, C. N. H., and Engel, F. L.: Biochemical Studies on Shock: Role of Peripheral Tissues in Metabolism of Protein and Carbohydrate During Hemorrhagic Shock in Rat, *J. Exper. Med.* **79**: 1-7 (Jan.) 1944. Engel, F. L.; Harrison, H. C., and Long, C. N. H.: Biochemical Studies on Shock: Role of Liver and Hepatic Circulation in Metabolic Changes During Hemorrhagic Shock in Rat and Cat, *ibid.* **79**: 9-22 (Jan.) 1944. Russell, J. A.; Long, C. N. H., and Wilhelmi, A. E.: Biochemical Studies on Shock: Oxygen Consumption of Liver and Kidney Tissue from Rats in Hemorrhagic Shock, *ibid.* **79**:23-33 (Jan.) 1944. (b) Shen, S. C., and Ham, T. H.: Studies on Destruction of Red Blood Cells, *New England J. Med.* **229**:701-713 (Nov. 4) 1943. (c) Govier, W. M.: Studies on Shock Induced by Hemorrhage: III. The Correlation of Plasma Thiamin Content with Resistance to Shock in Dogs, *J. Pharmacol. & Exper. Therap.* **77**:40-49 (Jan.) 1943. (d) Aub, J. C.; Brues, A. M.; Dubos, R.; Kety, S. S.; Nathanson, I. T.; Pope, A., and Zamecnik, P. D.: Bacteria and the Toxic Factor in Shock, *War Med.* **5**:71-73 (Feb.) 1944. (e) Prinzmetal, M.; Freed, S. C., and Kruger, H. E.: Pathogenesis and Treatment of Shock Resulting from Crushing of Muscle, *ibid.* **5**: 74-79 (Feb.) 1944. (f) Glenn, W. L.; Muus, J., and Drinker, C. K.: Observations on the Physiology and Biochemistry of Quantitative Burns, *J. Clin. Investigation* **22**:451-459 (May) 1943. Perlmann, G. E.; Glenn, W. W., and Kaufman, D.: Changes in Electrolytic Pattern in Lymph and Serum in Experimental Burns, *ibid.* **22**:627-633 (July) 1943. (g) Ricca, R. A.; Fink, K.; Katzin, L. I., and Warren, S. L.: Effect of Environmental Temperature on Experimental Traumatic Shock in Dogs, *J. Clin. Investigation* **24**:127-139

11. Scudder, J.: Shock: Blood Studies as a Guide to Therapy, Philadelphia, J. B. Lippincott Company, 1940.

12. Bywaters, E. G. L., and Popjak, G.: Experimental Crushing Injury, *Surg., Gynec. & Obst.* **75**:612-627 (Nov.) 1942. Bywaters, E. G. L.: Ischemic Muscle Necrosis, *J. A. M. A.* **124**:1103-1109 (April 15) 1944. Clarke, A. P. W., and Cleghorn, R. A.: Chemical Studies of Tissue Changes in Adrenal Insufficiency and Traumatic Shock, *Endocrinology* **31**:597-606 (Dec.) 1942.

(Footnote continued on next page)

## RESULTS

None of the animals showed gross evidence of active peritonitis or fat necrosis, although local adhesions about the pancreaticoenterostomy were pronounced in 4 (18 per cent) and moderate in 11 (50 per cent); in the remaining 7 (32 per cent), adhesions were slight or absent. Other significant observations are summarized in the table.

*Response to Secretin.*—Of the 22 animals studied, 15 showed definite secretion of pan-

Among the 6 remaining failures, dogs 4, 5 and 12 were tested within nine days of the operation. Despite the negative response of dogs 4 and 5, microscopic sections showed that a junction had been made between the pancreatic duct and the jejunal mucosa, while dog 12 showed acute pancreatitis and no evidence of fistula. Two other negative responses occurred, in dogs 7 and 8, investigated at twenty-one and twenty-six days respectively. Microscopic sections in these animals revealed diffuse fibrosis of the pancreatic

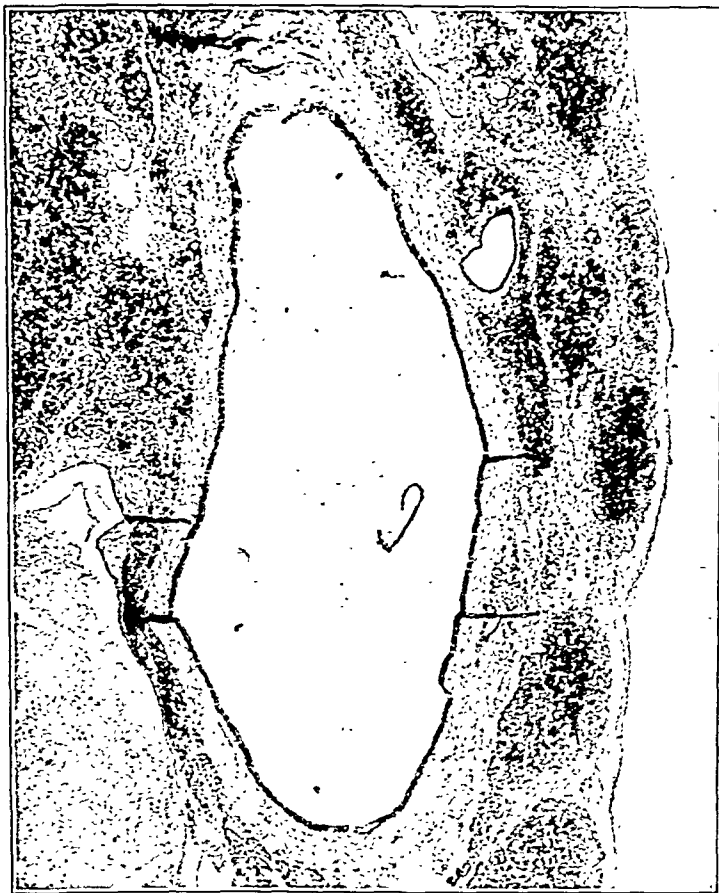


Fig. 2.—Pronounced dilatation of the duct due to obstruction from fibrosis. Note the flattened epithelial lining and the moderate degree of parenchymal scarring ( $\times 40$ ).

creatic juice at the pancreaticojejunal junction after intravenous injection of secretin, an incidence of spontaneous fistula formation of 68 per cent. One (dog 11) died of air embolism immediately after the injection of secretin into the vena cava, so that no determination of the secretory response could be made. Elimination of this animal from the series would result in an incidence of 71 per cent of spontaneous fistula formation.

stump, failure of the duct to form a junction with the jejunal mucosa and pronounced dilatation of the duct system (fig. 2). In the last failure, dog 9, a large retention cyst of the implanted stump developed, containing fluid which gave a strongly positive reaction for amylase.

*Acute Pancreatitis.*—Microscopic studies of the implanted pancreatic stumps revealed some evidence of acute inflammatory reaction in 6 animals; an incidence of 27 per cent. As noted in the table, pronounced diffuse pancreatitis was

Therapy in most experiments on burns and tourniquet shock was begun one-half to one hour after the injury, when visible symptoms of shock, namely prostration and dyspnea, were present. Deaths in untreated animals had already occurred at the time therapy was begun. Even when therapy was delayed beyond this point, favorable responses to administration of saline solution have been obtained. In hemorrhage experiments 10.5 per cent of the mice had died at the time of onset of therapy, which was administered in the interval between bleedings (after a blood loss of 2.25 per cent body weight).

The percentage of survivors is considerably lower if only 5 per cent of body weight of an isotonic solution of a sodium salt is given (chart 4); this, in part, explains the lack of

ion. A similar response was obtained with all the sodium salts we have tested, while other cations—potassium, calcium, magnesium, cesium, rubidium and lithium—were either deleterious or without effect.<sup>25</sup>

Likewise, isotonic dextrose solutions had little effect (chart 5); given intraperitoneally (and this probably applies to other methods of administration such as hypodermoclysis), they were decidedly harmful<sup>5</sup> because they temporarily withdrew water and sodium from the body. Hypertonic solutions in general were found to be less effective than isotonic solutions, perhaps for the same reason.

Water administered orally, 8 to 10 per cent body weight, was ineffective in burn shock (91 per cent mortality in 50 mice as compared with 95 per cent in 50 controls). In tourniquet

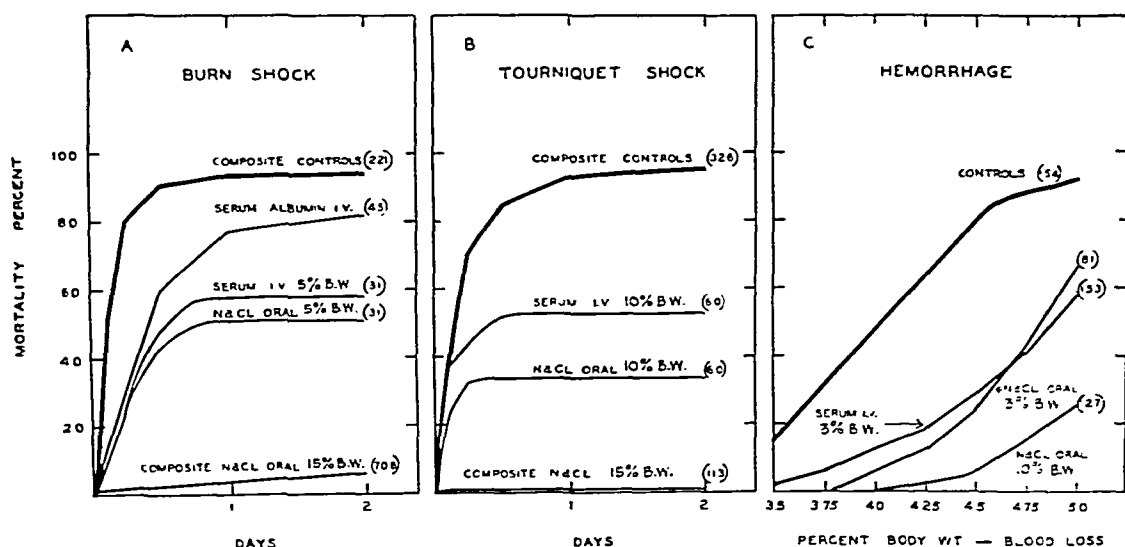


Chart 4.—The similar therapeutic response of mouse serum administered intravenously and saline solution administered orally in burn and tourniquet shock and hemorrhage, given in equivalent doses on a basis of body weight (B.W.). Concentrated human serum albumin (25 per cent) is less effective than serum in doses with equivalent protein content but less sodium chloride. Also the increased effectiveness of larger doses of isotonic solution of sodium chloride (10 to 15 per cent body weight) is indicated. Each curve is a composite of results of several experiments. Figures in parentheses indicate number of mice represented.

success with saline therapy frequently reported from the laboratory and clinic, where this amount has usually represented the maximum therapeutic dose.

A comparison of various salts has shown that the beneficial effect is a function of the sodium

ship of Salt Solutions, Serum and Defibrinated Blood in the Treatment of Severely Scalded, Anesthetized Dogs, *Ann. Surg.* 120:367-376 (Sept.) 1944.

24. Locke, W.: An Experimental Method for Evaluating Blood Substitutes, *Science* 99:475-476 (June 9) 1944.

25. Harkins, H. N.: Personal communication to the authors.

shock some benefit from this was seen (50 per cent mortality in 48 mice as compared with 90 per cent in 48 controls). In hemorrhage only slight benefit from water was obtained,<sup>4</sup> and this was shown to be due to blood dilution: in terms of hemoglobin loss, the animals treated with water were able to withstand no greater depletion than the controls.

Fruit juices, because of their high potassium content, are definitely harmful in experimental shock. An experiment in tourniquet shock demonstrated that 5 per cent body weight of

26. Rosenthal,<sup>2a</sup> Tabor and Rosenthal.<sup>5</sup>

into the ascending colon. If the intussusception becomes compound, then the clinical picture is that of intestinal obstruction.

The treatment of intussusception of the appendix into itself is appendectomy. In the event of a completely intussuscepted appendix, the appendix is removed by resecting a small cuff of cecum which surrounds the base of the appendix. The compound variety may be easily reduced, but if gangrenous, resection of a portion of the cecum and anastomosis of the ileum to the ascending or transverse colon are required.

#### REPORT OF A CASE

A 45 year old bipara was seen by a physician three years prior to operation for severe pain of twelve hours' duration in the right lower quadrant. The sudden acute pain was associated with nausea, vomiting and abdominal tenderness. Physical examination demonstrated tenderness without spasm in the right lower quadrant, a normal uterus and normal vaults. Her white blood cell count was 22,500, blood pressure 96 systolic and 60 diastolic and pulse rate 64. The urine was normal. Her pain and tenderness subsided in forty-eight hours, and she was well until one month later, when a similar pain in the right lower quadrant of the abdomen occurred. During the next six months she was free of pain, and physical examination revealed no abnormalities on three occasions. Two years later the pain recurred, associated with a slight fever. Still later the patient was referred to us. We found nothing abnormal on abdominal examination but an enlarged uterus. There was a large cystic mass in the right vault. On Nov. 24, 1943, with the patient under nitrous oxide, oxygen and ether anesthesia, an appendectomy, total hysterectomy and bilateral salpingo-oophorectomy were performed. The appendix was short and broad, and the junction of the appendix and cecum was unusually wide, measuring 1.5 cm. Because of its wide base, the appendix was removed between two Kocher clamps and the stump closed with two rows of chromic surgical gut stitches. Both ovaries were destroyed by large endometriomas which were adherent to a uterus containing fibroids and also to the under surfaces of the broad ligaments. The patient made an uneventful recovery.

*The Specimen.*—The distal half of the appendix had intussuscepted into the proximal half, and the invaginated mucosal surface of the tip of the appendix was smooth and glistening and was not ulcerated. The inverted end filled the wide lumen of the appendix, and the tip lay almost at the junction of the appendix and the cecum. In the accompanying drawing the wide base of the appendix is illustrated, as is the relationship between



Showing the wide base of the appendix and the relationship between appendix and cecum. At lower right the slight dimple at the end of the appendix is shown.

the cecum and the appendix. An end on view of the appendix is shown to demonstrate the slight dimple present, and on either side of the dimple there were bluish spots which were undoubtedly small endometriomas. Because of the loss of the appendix before microscopic examination, the diagnosis of endometriosis cannot be substantiated.

The first attack of pain, three years before operation, was undoubtedly acute appendicitis. This inflammatory process may well account for the subsequent development of the intussusception. The recurrence of the pain which necessitated further examination and operation in all probability was due to the intussusception, although the large endometriomas may have played some part in the production of the abdominal pain.

protein-free ultrafiltrate of serum along with the same serum and also by comparison of serum given by mouth (whereby the proteins as such would not be absorbed) with serum administered intravenously. In these experiments<sup>28</sup> likewise, the therapeutic response could be attributed to the electrolytes contained in the serum (chart 5A). The results with serum albumin (human) were inferior to those with saline solution or serum and here, again, could be correlated with the amount of electrolyte solution (isotonic solution of sodium chloride) contained in the preparation (chart 4A).

In contrast to the absence of influence of administration of serum protein was the better therapeutic effect observed in hemorrhage when whole blood or erythrocytes in isotonic solution of sodium chloride were compared with plasma or saline solution alone (chart 5C).

We have carried out similar studies with whole blood therapy for traumatic and burn shock and were unable to demonstrate any superiority over plasma or isotonic solution of sodium chloride similarly administered. In tourniquet shock, treatment with whole blood, 5 per cent body weight intravenously, brought about a survival of 35 per cent of 32 mice while with plasma 40 per cent survived. In burn shock, similar treatment with whole blood resulted in 42 per cent survivals as compared with 66 per cent with plasma. Thirty to 32 mice were employed in each group, and the control mortalities (untreated mice) were 100 per cent in both experiments.<sup>29</sup>

It is thus observed that under these experimental conditions therapy with whole blood is of value in hemorrhage, but in burn or traumatic shock no superiority over plasma or saline solution could be demonstrated. These observations are of particular interest in view of the recent use of whole blood in the treatment of all forms of shock.

#### OTHER FACTORS

Brief mention will be made of some other factors which we have studied in shock. The harmful effect of an environmental temperature that is too hot or too cold is now well recognized<sup>30</sup>; the exact optimum remains to be

established but available evidence indicates that it lies between 16 and 24 C.<sup>30a</sup>

Administration of 100 per cent oxygen at atmospheric pressure did not affect mortality of burn or tourniquet shock in mice<sup>29</sup>; Frank and Fine have previously reported negative results with oxygen at a pressure of 3 atmospheres for dogs.<sup>31</sup> Morphine in analgesic doses (2 to 6 mg. per kilogram) had no unfavorable influence on burn shock in mice<sup>29</sup>; Blalock has previously reported similar results in dogs.<sup>32</sup> Injection of adrenal cortex extract either prophylactically or subsequent to burns did not affect the acute mortality. Likewise, no therapeutic effect was observed from therapeutic doses of epinephrine in oil or from posterior pituitary extracts.<sup>2b</sup> In local therapy of burns, covering two thirds or more of the body surface with tannic acid, liquid petrolatum or cod liver oil was deleterious in that the mortality from shock was increased.<sup>2a</sup>

The immunity which has been observed after repeated trauma has been shown to be a local tissue response rather than a humoral reaction.<sup>33</sup>

#### COMMENT

With simplified procedures it has been possible to study the acute mortality following burns, trauma and hemorrhage in large numbers of small animals. The correction of disturbances of fluids and specific electrolytes has been demonstrated to be of greater importance for survival than the administration of plasma proteins. Our results indicate that for the most favorable response quantities of isotonic solutions of sodium salts equal at least to 10 per cent of body weight are indicated during the first twenty-four hours. In this respect, it is believed that current methods of treating shock are inadequate.

by Environmental Temperature, *Proc. Soc. Exper. Biol. & Med.* **51**:350-351 (Dec.) 1942. Rosenthal.<sup>2a</sup> Ricca, Fink, Katzin and Warren.<sup>14f</sup>

30a. More recent studies of temperature effects<sup>29</sup> have shown that the increased survival time of untreated animals kept at 16 to 22 C. is not a true criterion of optimum temperature. When mice with tourniquet shock are treated with adequate amounts of isotonic solution of sodium chloride or plasma, an entirely different response is obtained; the majority of them will live if kept at 26 to 29 C., while the majority of them will die if kept below 22 C. or above 31 C.

31. Frank, H. A., and Fine, J.: Traumatic Shock: V. A Study of the Effect of Oxygen on Hemorrhagic Shock, *J. Clin. Investigation* **22**:305-313 (March) 1943.

32. Blalock, A.: Effects of Morphine in Experimental Shock Due to Hemorrhage, *Arch. Surg.* **47**:326-328 (Oct.) 1943.

33. Rosenthal, S. M.; Tabor, H., and Lillie, R. D.: The Local Nature of Acquired Resistance to Trauma, *Am. J. Physiol.* **143**:402-406 (March) 1945.

28. Rosenthal.<sup>3</sup> Tabor, Kabat and Rosenthal.<sup>4</sup>

29. Unpublished results.

30. Gatch, W. D., and Wakim, K. G.: Effect of External Temperature on Shock: Experimental Study, *J. A. M. A.* **121**:903-907 (March 30) 1943. Cleghorn, R. A.: The Effect of Different Environmental Temperatures on the Survival of Dogs After Severe Bleeding, *Canad. M. A. J.* **49**:363-367 (Nov.) 1943. Elman, R.; Cox, W. M.; Lischer, C., and Mueller, A. J.: Mortality in Severe Experimental Burns as Affected

Holm<sup>19</sup> calls attention to the lines formed in growing bones as a result of phosphorus poisoning and shows by roentgenograms that they may last a lifetime.

*Ligaments, Muscles and Tendons.*—Kuhns<sup>20</sup> points out that ligamentous weakness is present and easily discernible as a clinical entity in 10 per cent of children but that ligamentous tightness is also present in many and has received scant attention. Tightness is found more frequently in the hamstring and back areas.

Goldberg and Comstock<sup>21</sup> emphasize the differential diagnosis of herniations of muscle observed in the legs from lipoma, hematoma, tuberculosis, pseudo hernia and varices. A case of multiple small hernias of the tibialis anterior muscles of both legs is presented.

In an analysis of 190 cases of chronic non-specific tenosynovitis and peritendinitis, Lipscomb<sup>22</sup> feels that trauma is in most instances the etiologic factor. The pathologic changes are reviewed, and his opinion is that they differ only in degree and depend on the duration of the disease primarily. Conservative treatment consisting in splinting and roentgen ray therapy is advised, and if improvement does not occur surgical intervention is indicated.

19. Holm, O. F.: Beitrag zur Kenntnis der Entstehung der Phosphorsklerose, *Acta radiol.* **23**:549-561, 1942.

20. Kuhns, J. G.: Tightness of Ligamentous Structures, *Arch. Pediat.* **61**:179-183 (April) 1944.

21. Goldberg, H. C., and Comstock, G. W.: Herniation of Muscles of the Legs, *War Med.* **5**:365-367 (June) 1944.

22. Lipscomb, P. R.: Chronic Nonspecific Tenosynovitis and Peritendinitis, *S. Clin. North America* **24**:780-797 (Aug.) 1944.

*Osteochondritis.*—Uhry<sup>23</sup> presents an interesting review of 79 cases of osteochondrosis of the tuberosity of the tibia (Osgood-Schlatter's disease) and defends the original ideas of the persons first describing the condition in which the disorder develops as a result of minor separation of the structures of the tibial tubercle and the patellar ligament. The author believes that the characteristic pathologic changes represent callus repair at the site of separation. He feels that osteochondritis as such (that is, inflammation) is not in evidence. The immediate instigating factor is consistently trauma.

*Sudeck's Atrophy.*—Buchman<sup>24</sup> reports an interesting case of Sudeck's atrophy following a single minor surgical procedure for exploration of a tendon sheath. The surgical treatment was followed by severe symptoms, partially relieved by injection of procaine hydrochloride after lack of response to usual methods of treatment.

*Abuse of Bed Rest.*—Since this article will probably not come within the purview of the editors of other sections of "Progress in Orthopedic Surgery," it is felt that it should be mentioned here. Ghormley<sup>25</sup> sounds a keynote of change from the emphasis placed on rest by Hugh Owen Thomas and cites the many disadvantages of rest as compared with early activity in the orthopedic field.

23. Uhry, E., Jr.: Osgood-Schlatter Disease, *Arch. Surg.* **48**:406-414 (May) 1944.

24. Buchman, J.: Postoperative Post-Traumatic Osteoporosis or Sudeck's Atrophy, *Bull. Hosp. Joint Dis.* **4**:55-61 (Oct.) 1943.

25. Ghormley, R. K.: Abuse of Rest in Bed in Orthopedic Surgery, *J. A. M. A.* **125**:1085-1087 (Aug. 19) 1944.

## II. CONGENITAL DEFORMITIES

PREPARED BY J. HIRAM RITE, M.D., ATLANTA, GA.

For several years I have begun this section on "congenital deformities" with a description of the experiments conducted by Josef Warkany. Each year he and his workers have given additional information on the cause of some of the congenital deformities. This past year has brought information on how to prevent deformities.

In times past, various authors have attributed congenital malformations to a maternal nutritional deficiency. Warkany and Schraffenberger,<sup>26</sup> after establishing a set pattern of deformities which follow what they call diet I, made

various additions to the diet, trying to prevent deformities. They found first that 2 per cent pig liver would prevent deformities. A search was made for the preventive factor in pig liver. After studying hundreds of litters of rats, they give the following conclusions:

The congenital malformations of the pattern of diet I are prevented when the maternal diet I is supplemented by riboflavin. Supplements of thiamine hydrochloride, nicotinic acid, pyridoxine and calcium pantothenate are not preventive. With a purified maternal diet in which the vitamin B complex is represented by crystalline substances, malformations of the pattern of diet I appear in the offspring when riboflavin is omitted. On the same diet supplemented by

26. Warkany, J., and Schraffenberger, E.: Congenital Malformations Induced in Rats by Maternal Nutritional Deficiency, *J. Nutrition* **27**:477 (June) 1944.

# GELATIN SPONGE. A NEW HEMOSTATIC SUBSTANCE

## STUDIES ON ABSORBABILITY

HILGER PERRY JENKINS, M.D., AND JAMES S. CLARKE, M.D.

CHICAGO

Hemostasis is a fundamental principle in surgical technic. It can be satisfactorily obtained in most instances by ligature, clips, pressure, electrocoagulation and packs. There are some situations, however, in which venous or capillary bleeding may be difficult to control by these methods. This is especially true of neurosurgical operations in which bleeding from the dura, the brain or the spinal meninges may be especially troublesome. This also obtains in many instances of general surgical procedures, such as operations on liver, kidney, spleen, pancreas, thyroid, bone, chest and female generative tract, in which conventional hemostatic methods may not be adequate. Ways and means of obtaining better hemostasis in such circumstances would constitute a substantial improvement in the general technic of surgery.

The major recent advances in the problem of control of capillary and venous oozing have been the development of coagulating agents, such as thrombin, and the use of absorbable substances which will aid in clot formation by purely mechanical means, such as transmitting pressure to the bleeding surface and offering a matrix for the formation of the clot. The clot-forming properties of these substances are presumed to be enhanced by the addition of the thrombin. The use of muscle stamps, which was introduced by Cushing<sup>1</sup> in 1911 and has been rather widely used in neurosurgical procedures since that time, constitutes the first general use of these principles, in that the muscle transmits some pressure, is absorbed and contains a clot-promoting substance.<sup>2</sup>

From the Department of Surgery, University of Chicago, The School of Medicine.

This work was aided in part by a grant from The Upjohn Company, Kalamazoo, Mich.

1. Cushing, H.: The Control of Bleeding in Operations for Brain Tumors, with the Description of Silver Clips for the Occlusion of Vessels Inaccessible to the Ligature, *Ann. Surg.* **54**:1, 1911.

2. Fonio, A.: Ueber die Wirkung der intravenösen und der subkutanen Injektion von Koagulen Kocher-Fonio am Tierversuch, nebst einigen therapeutischen Erfahrungen, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **27**:642, 1914.

The work of Seegers<sup>3</sup> and his co-workers deserves special mention as a major contribution to the problem of hemostasis. They have developed a method of preparing a purified thrombin, which is now commercially available, and, furthermore, they have worked out a method of calibration and standardization of the potency of the thrombin known as the Iowa unit. There have been commercial preparations of thrombin or clot-promoting substances obtained from muscle or tissue extracts which have been available on the market for many years. This type of material has been outmoded, however, since the work of the Iowa group.

From the standpoint of absorbable substances which could mechanically aid in the formation of a clot, the work of Frantz<sup>4</sup> deserves attention. She found that oxidized cellulose in the form of absorbable cotton, paper or gauze was absorbed in eleven to thirty days in dogs and cats and produced only a mild foreign body reaction. She and co-workers reported the successful use of oxidized cellulose without thrombin to control bleeding in 17 cases in which muscle would otherwise have been required for hemostasis. Putnam<sup>5</sup> used oxidized cellulose soaked in thrombin to control bleeding in thirty neurosurgical operations and found it satisfactory. Cronkite, Deaver and Lozner<sup>6</sup> have been favorably impressed with the use of thrombin with and without oxidized cellulose to arrest hemorrhage in operative and traumatic wounds. The observations of Uihlein

3. Seegers, W. H.; Warner, E. D.; Brinkhouse, K. M., and Smith, H. P.: The Use of Purified Thrombin as a Hemostatic Agent, *Science* **89**:86, 1939. Seegers, W. H., and Doub, L.: Oxidized Cellulose and Thrombin, *Proc. Soc. Exper. Biol. & Med.* **56**:72, 1944.

4. Frantz, V. K.: Absorbable Cotton, Paper and Gauze, *Ann. Surg.* **118**:116, 1943. Frantz, V. K.; Clarke, H. T., and Lattes, R.: Hemostasis with Absorbable Gauze, *ibid.* **120**:181, 1944.

5. Putnam, T. J.: The Use of Thrombin on Soluble Cellulose in Neurosurgery, *Ann. Surg.* **118**:127, 1943.

6. Cronkite, E. P.; Deaver, J. M., and Lozner, E. L.: Experiences with Use of Thrombin With and Without Soluble Cellulose for Local Hemostasis, *War Med.* **5**:80 (Feb.) 1944.



bell and Grice,<sup>37</sup> from Boston, describe the modification of the Denis Browne splint for the treatment of congenital club feet. They use a splint which is narrower in the heel and makes the foot better and is also arched to prevent the rocker bottom. They have made an improvement in the method of strapping the foot to the splint. They give the following summary:

During the treatment of 53 patients with complicated congenital talipes equinovarus with the modified Denis Browne splint, several refinements in technic have been evolved to meet various problems, such as pressure sores, dermalis, incomplete correction, persistent equinus deformity, loss of longitudinal arch and unilateral deformity. These refinements are described. Success of this method depends on the accuracy with which the foot is fixed to the splint. If properly applied, the splints will allow correction

of the varus deformity and yet will maintain the longitudinal arch while obtaining full correction of the equinus deformity. Recurrence of the deformity is a constant threat, but this tendency is minimized by complete correction early and then by continued use of the splint intermittently, at least until the child begins to walk.

[ED. NOTE (J. H. K.).—For the last two years I have commented at length on my experiences with the Denis Browne splint. Briefly, I have obtained better results with plaster. I have tried the method of strapping mentioned by the author and feel that it is an improvement. Denis Browne says that he has made more than fifty modifications of the splint. Still more may be expected.]

[ED. NOTE (L. D. B.).—I have seen Grice apply the modified splint and have seen several of the patients. The splint and the method of applying the adhesive are great improvements in the Denis Browne technic, and any one using splint therapy should adopt these modifications.]

37. Bell, J. F., and Grice, D. S.: Treatment of Congenital Talipes Equinovarus with the Modified Denis Browne Splint, *J. Bone & Joint Surg.* 26:799 (Oct.) 1944.

### III. TUMORS OF BONE AND OF SYNOVIAL MEMBRANE

PREPARED BY HENRY W. MEYERDING, M.D., ROCHESTER, MINN.

*A. Classification of Tumors of Bone.*—Brachetto-Brian<sup>38</sup> presents a classification adopted by the "Comité para el Estudio de los Tumores Oseos" of the Asociación Argentina de Cirugía.

He discusses various phases and believes that the classification should be based on the type of tissue affected, since different cells would originate different neoplasms. The classification is as follows:

	Genetic Cells	Neoplasms Originated		Names of Tumors
A. Tumors of the skeletal sector	Osteoblast	I. Osteoblastoma	Benign Malignant	Osteoma Osteosarcoma; osteogenic sarcoma
	Chondroblast	II. Chondroblastoma	Benign Malignant	Chondroma Chondrosarcoma
	Myeloplax	III. Myeloplaxoma	Benign Malignant	Giant cell tumor
B. Tumors of the reticulo-endothelial sector	Mesoblast Histioocyte Reticuloblast Angioblast	IV. Reticuloblastoma	Benign Malignant	Reticulosarcoma Ewing's sarcoma
C. Tumors of the hemato-poietic sector	Mesoblast Hemohistioblast Hemocytioblast	V. Myeloblastoma		Kahler's disease; myeloma
D. Tumors of the vasculo-connective sector	Mesoblast Fibroblast Angioblast	VI. Fibroma and so forth	Benign	
		VII. Osteosarcoma	Malignant	

In the following tabulation these seven groups of neoplasms are represented with their varieties:

A. Tumors of the skeletal sector	I. Osteoblastoma	Benign	1. Benign osteoblastoma of the substantia spongiosa 2. Benign sclerosing osteoblastoma 3. Benign chondro-osteoblastoma
		Malignant	1. Malignant osteogenic osteoblastoma 2. Malignant osteogenic osteoblastoma with myeloplaxes 3. Secondary malignant osteogenic osteoblastoma 4. Juxtaconjugal malignant osteogenic osteoblastoma 5. Telangiectatic malignant osteogenic osteoblastoma
	II. Chondroblastoma	Benign	1. Chondroblastoma 2. Chondromyxoblastoma
		Malignant	1. Malignant chondroblastoma
B. Tumors of the reticulo-endothelial sector	III. Myeloplaxoma	.....	1. Benign myeloplaxoma 2. Malignant myeloplaxoma
			1. Localized reticuloendothelioma
	IV. Reticuloblastoma	Benign	
		Malignant	1. Undifferentiated reticulosarcoma 2. Differentiated reticulosarcoma

38. Brachetto-Brian, D.: La clasificación adoptada en el "comité para el estudio de los tumores oseos." *Revista méd. argent.* 28:2185-2190 (Nov. 19) 1941;

abstracted, *Arch. cubanos cancerol.* 3:19-26 (Jan.-March) 1944.

The most recent of the absorbable hemostatic materials is gelatin sponge or foam.<sup>11</sup> This is prepared from ordinary commercial gelatin, which is made up in a solution, to which a hardening agent is added. After bubbles of air are introduced, the mixture is allowed to dry in pans. It can then be cut into any desired size or shape. The material which has been used for experimental purposes has been provided in sealed glass jars previously subjected to sterilization with dry heat. The gelatin sponge is a white crisp material which is extremely light in weight. One cubic centimeter weighs 9 mg. The sponge will take up many times its weight of water when it is submerged and the air bubbles expressed.

additional factor in this evaluation, the gelatin sponge was used without thrombin.

A series of 12 dogs was operated on by ordinary aseptic surgical technic with ether anesthesia. After the abdomen had been opened, incisions were made 2 cm. long and 1 cm. deep in the liver, the kidneys and the spleen. The brisk hemorrhage which resulted from these incisions was controlled by packing the moistened gelatin sponge into the incision and holding it in place for about two minutes with ordinary moistened gauze. When the gauze was removed, the gelatin sponge was usually adherent in the incision and the bleeding stopped. Sometimes there was oozing from the ends of the incision, which was arrested by laying another piece of gelatin sponge over the length of the incision and covering the previously applied sponge. Gelatin sponge was also implanted in the

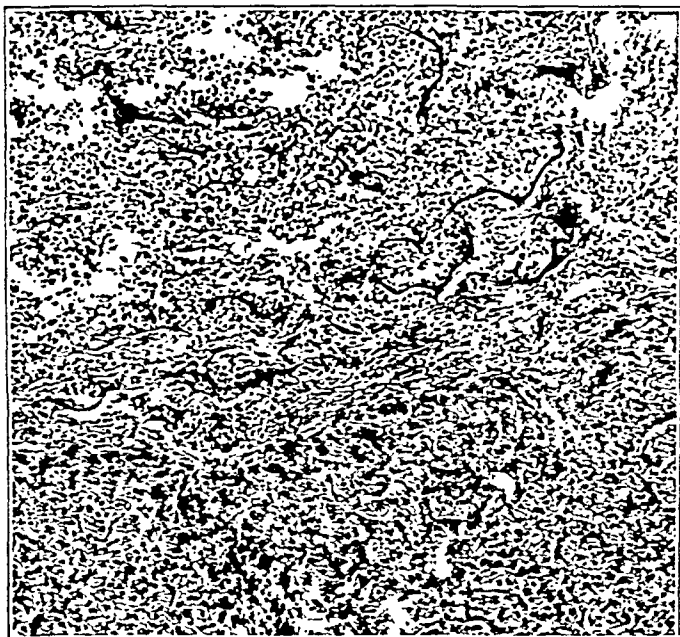


Fig. 2.—Gelatin sponge in liver after seven days. There is a wide zone of polymorphonuclear leukocytic invasion of the sponge at its junction with the liver, the parenchyma of which does not appear to exhibit any inflammatory reaction. The sponge appears to have undergone a considerable degree of absorption, as only fragments remain near the liver.

When moistened, the gelatin sponge shrinks and becomes soft and pliable. It easily adjusts itself to any irregularities in the surface to which it is applied. It does not fragment easily, although it is not especially tough.

#### EXPERIMENTAL STUDY

An experiment was devised primarily to determine the behavior of the gelatin sponge in the tissues of animals and the response of the tissues to the gelatin. To avoid the introduction of an

omentum and in the rectus muscle near the abdominal incision. The animals were killed at periods varying from two to fifty-six days after the implantation. Two of the animals died at two and three days respectively.

At autopsy the sponge could usually be easily identified in the short term implants as a red soggy mass. In the omentum there was an area of induration, in the center of which the sponge could be found if the omentum was cut across at this point. In the abdominal wall one could usually detect a small area of induration along the peritoneal surface (the sponge was put between the posterior sheath and the rectus muscle) which when cut revealed the sponge. After a week or ten days it was often difficult to

11. Correll, J. T., and Wise, E. C.: Certain Properties of a New Physiologically Absorbable Sponge, *Proc. Soc. Exper. Biol. & Med.* 58:233, 1945.

which the pathologic report was osteosarcoma. Subsequent to this, fracture of the third metatarsal bone with callus formation developed. Excision was again requested, and the lesion proved to be benign march fracture with callus formation. Still later the patient had fractures of the first and fourth metatarsal bones, which were evident on roentgenographic examination. At the time the paper was written, he was living and working in a lumber mill fourteen years following operation on the second metatarsal bone. The specimen and the tissues were reexamined by Dr. Broders and showed unquestionably that the original lesion of the second metatarsal bone was osteosarcoma and that the lesion of the third metatarsal bone was march fracture.

Gershon-Cohen and Doran<sup>64</sup> review the literature of fatigue-stress fractures and emphasize the necessity for ruling out systemic disease and local pathologic changes. They support the hypothesis of fatigue-stress and present 4 cases. They state that the fracture lines are thin and the callus formation is diagnostic, although they believe that the lesion could be taken for osteogenic sarcoma in the latter stages of the condition.

[ED. NOTE.—My case reported at the beginning of this section illustrates the confusion which could arise by depending on roentgen interpretation alone.]

Friedman<sup>65</sup> reports a case of osteolytic osteogenic sarcoma of the os pubis, which is an extremely rare location. His patient was a woman 42 years of age. Roentgenographic examination revealed destruction of the right horizontal ramus of the pubic bone. The serum alkaline phosphatase was elevated to 18 units; the calcium and phosphorus levels were normal. A biopsy was done, and the pathologist's diagnosis was osteolytic osteogenic tumor of bone. Roentgen therapy was given for thirty-one months, with no essential change in the roentgenograms. The patient died of metastasis three and a half years later.

[ED. NOTE.—The very rare location of the lesion in this case, in which a thorough study of the microscopic and roentgenologic findings was made and the end result was obtained, makes reports of this type of value. My statistical studies of tumors of bone have been based on facts obtained from proved microscopic changes, histopathologic determination of the grade of malignancy and subsequent follow-up of cases.

64. Gershon-Cohen, J., and Doran, R. E.: Fatigue-Stress Fractures: Diverse Anatomic Location and Similarity to Malignant Lesions, *U. S. Nav. M. Bull.* 43: 674-684 (Oct.) 1944.

65. Friedman, S. T.: Osteogenic Osteolytic Sarcoma of the Os Pubis, *Am. J. Surg.* 64:248-253 (May) 1944.

Statistical reports without a report of the microscopic studies are not based on sufficient evidence of proof of malignancy and therefore are of less value in determining the benefits of treatment and prognosis than those based on microscopic studies.]

McNattin,<sup>66</sup> stimulated by the lack of satisfactory opinions concerning any one method of treatment of osteogenic sarcoma, reports a small series of cases in which the patients were treated by roentgen rays for from sixty to one hundred and forty treatments. The treatments were given over multiple portals, and amputation was done when the first signs of irradiation necrosis appeared. He believes that this form of therapy gives the best prognosis and that delay of amputation does not increase the likelihood of distant metastasis. He believes that if serial roentgenograms show some recession of the lesion, indicating radiosensitivity in this type of sarcoma, the total amount of irradiation may be decreased and amputation may be avoided.

[ED. NOTE.—Treatment by means of roentgen rays given preoperatively followed by amputation (Ferguson) delays removal of a malignant lesion. Such a delay is contrary to the common belief that early eradication is the method of choice. Unless there is microscopic proof of the grade of malignancy, I hardly feel that the results of treatment of osteogenic sarcoma by roentgen therapy alone are acceptable.]

Osteochondrosarcoma: Haggart, Hare and Marks<sup>67</sup> present a case in which osteochondrosarcoma arose from the rami of the pubis and ischium. The surgical removal of the tumor was made difficult by its location, since it was adjacent to and compressing the rectum.

Kemper and Bloom<sup>68</sup> present a case of osteochondrosarcoma. The patient was a girl, 13 years of age. Biopsy revealed a spindle cell osteochondrosarcoma of the right tibia without metastasis, and amputation through the lower part of the thigh was done. Two years subsequently there was an osteochondrosarcoma of the femur. At this time a midthigh amputation was done. Then about five months later a maxillary tumor, a mass in the upper right quadrant of the abdomen and recurrence of the osteochondrosar-

66. McNattin, R. F.: Treatment of Osteogenic Sarcoma with Preoperative Roentgen Radiation in Large Doses, *Radiology* 42:246-248 (March) 1944.

67. Haggart, G. F.; Hare, H. F., and Marks, J. H.: Clinico-Pathological Conference [Osteochondrosarcoma], *Radiology* 43:378-382 (Oct.) 1944.

68. Kemper, J. W., and Bloom, H. J.: Metastatic Osteochondroma of Maxilla from Primary Tumor of Tibia: Report of Case, *Am. J. Orthodontics (Oral Surg. Sect.)* 30:704-708 (Nov.) 1944.

however, there was only a slight invasion of the sponge by polymorphonuclear leukocytes. In addition, there were also lymphocytes and some plasma cells in the peripheral portions.

After a week or more, the predominant cells invading the gelatin sponge were macrophages. There was little tendency for the formation of foreign body giant cells, such as one sees frequently in microscopic sections of suture material such as cotton, silk, linen or chromic surgical

tion became fibrous. In the longer term implants, the fibrous tissue appeared to invade the periphery of the sponge where absorption had occurred as a result of the activity of the macrophages.

In some of the sections there was evidence of the surgical gut suture material which had been used to hold the implant in place. The tissue response to the gut was invariably more pronounced than that observed for the gelatin sponge.



Fig. 4.—Gelatin sponge in liver after twenty-three days. The gelatin sponge is separated from the normal-appearing liver cells by a thin zone of fibrous tissue which merges with and invades the peripheral portion of the sponge. The interstices of the sponge are filled with red blood cells in some areas, and there are a moderate number of macrophages throughout. Polymorphonuclear leukocytes are scarce. There is some thinning out of the walls of the cavernous spaces and some collapsing of the walls, indicative of a moderate degree of absorption.

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The absorption of the gelatin sponge was apparently most rapid in the presence of polymorphonuclear leukocytes, which appeared to produce a liquefaction of the gelatin sponge. In some such instances, the absorption had progressed almost to completion within twelve days. On the other hand, most of the implants showed evidence of a slower absorption, which appeared to be carried out by macrophages and which

stresses and strains. In coxa valga, the internal architecture undergoes a devolutionary change as a result of modification of the external form and is similar to that of the almost straight reptilian femur. In osteoarthritis, a new compact articular surface is formed superficial to the original one and supported by new trabeculated elements which continue the radiating lines of the original trabecular pattern. A devolutionary process, both in the external architecture and consequently in the internal architecture, takes place in the stumps of the amputated femurs after loss of the full normal function of weight bearing. In 2 specimens examined after amputation, there was an increase in the neck angle, a decrease in the length of the neck and displacement of the head of the femur laterally, backward and downward. The backward displacement represented a retorsion of the head on the neck and exposed the medial part of the anterior surface of the neck to pressure of the iliofemoral ligament and the anterior margin of the acetabulum, thus producing an extension of the articular surface of the head in this region.

Kleinberg<sup>89</sup> reports a case of aseptic necrosis of the femoral head following a dislocation which he believes was not associated with a tear of the round ligament. Exploration of the hip showed a normal-appearing ligamentum teres, grossly and microscopically. He believes that this case demonstrates that rupture of the ligamentum teres is not a constant occurrence in a traumatic dislocation. The author points out that in most cases in which the femoral head is deliberately dislocated from the acetabulum the round ligament is torn, but not infrequently the head can be removed from the acetabulum without rupturing the round ligament.

Salmore<sup>90</sup> measured the pelvifemoral angle in 100 normal persons and found that the most accurate measurements could be made with the patient in the erect position. This angle was defined by Milch as the backward opening angle formed by the axis of the femoral shaft with Nélaton's line; it is valuable in measuring the degree of hip flexion. It was found to be between 50 and 52 degrees in normal adults and children and 58 degrees in the preambulatory infant.

Wellmerling<sup>91</sup> discusses the management of fractures of the femoral neck in relation to certain anatomic considerations of the upper end of

the femur. There are two distinct systems of trabeculae arranged in curved paths, one beginning on the medial side of the upper femoral shaft and curving upward in a fanlike radiation to the opposite portion of the bone and the other originating in the lateral portion of the upper shaft, arching upward and medially. The result of the dense converging trabeculae is a thickened anterior and medial cortex. The fracture is reduced by overtraction in adduction and fixed in a coxa valga position, thereby interlocking the fragments and restoring the normal length. The author relies on his senses and insertion of a guide wire and cannulated nail, controlled by two plane roentgenography, rather than directing devices. For fixation he uses a 5 inch (12.7 cm.) cannulated, vitallium Smith-Peterson nail. The cortex is entered just posterior to the center of the lateral aspect of the shaft and 2 inches (5 cm.) distal to the distal prominence of the trochanter with a 5/32 inch (0.4 cm.) drill. The nail is driven with a 20 degree forward inclination so that it lies in the anteromedial wall of the neck, where the converging trabeculae are the most supportive. If the nail enters the midportion or anterior to it, the nail will emerge through the anterior portion of the neck. [Ed. NOTE.—In cases of oblique neck fractures with a spicule beneath the proximal fragment, abduction is usually necessary to accomplish reduction.]

Siris and Ryan<sup>92</sup> believe that the chances of survival are better in cases of intracapsular fractures of the neck of the femur when reduction is done immediately. The use of two machines has simplified the technic and makes draping easier. They do not permit the patients to turn on the uninjured side, because in a certain number of cases this has caused loosening of the nail.

Miller and Bishop<sup>93</sup> reported the case of a 76 year old patient with a fracture of the femoral neck, who died during manipulation of the hip while he was under cyclopropane anesthesia eighteen days following fracture. Autopsy revealed a pulmonary embolism which came from the femoral vein. The authors suggest that early reduction might reduce the incidence of this complication.

Weinberger<sup>94</sup> describes a method for converting fractures of the femoral neck into a valgus

89. Kleinberg, S.: Aseptic Necrosis of the Head of the Femur Following Dislocation of Hip, *Arch. Surg.* 49:104-108 (Aug.) 1944.

90. Salmore, W.: Pelvifemoral Angle, *J. Bone & Joint Surg.* 26:392-393 (April) 1944.

91. Wellmerling, H. W.: New Therapy of Hip-Nailing: Precision Technique for Intracapsular Fractures, *Indust. Med.* 13:809-817 (Oct.) 1944.

92. Siris, I. E., and Ryan, J. D.: Fractures of the Neck of the Femur: An Analysis of 157 Intracapsular and Extracapsular Fractures, *Surg., Gynec. & Obst.* 78:631-639 (June) 1944.

93. Miller, S., and Bishop, H. F.: Fatal Pulmonary Embolism During Manipulation of Hip Under Anesthesia, *Anesthesiology* 5:300-302 (May) 1944.

94. Weinberger, M.: Modification of Lines of Force in Treating Fractures of Neck, *Rev. brasil. de ortop. e traumatol.* 4:235-240 (Sept.-Dec.) 1943.

however, there was only a slight invasion of the sponge by polymorphonuclear leukocytes. In addition, there were also lymphocytes and some plasma cells in the peripheral portions.

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are not usually willing to accept it, and it is contraindicated when both hips are involved and when the spine is affected. Cup arthroplasty may offer hope of retaining motion and relieving pain in certain cases.

Bergmann<sup>110</sup> discusses aseptic bone necrosis in lesions of the hip. In fractures of the femoral neck, the arteries running along the inner lining of the capsule and entering the head are destroyed, leaving only the vessels of the round ligament, which are insufficient in most instances to keep the head from undergoing necrosis. The adjacent living bone of the distal fragment unites with the head before it has gone through all the stages of reorganization. The endosteum of the distal fragment is the only source from which new bone is laid down, and this is inferior to periosteal callus. The pathologic changes of Perthes' disease (osteochondrosis of the capital epiphysis of the femur), congenital dislocation of the hip and caisson disease are discussed and illustrated with roentgenograms and photographs. [Ed. NOTE (J. J. F.).—One interested in the pathologic changes of aseptic necrosis of the head of the femur should read this well illustrated article. In fractures of the femoral neck, there often remains a significant blood supply from the posterior capsular vessels.]

Stephens<sup>111</sup> reviews the literature on iliopectineal bursa and adds 2 cases to the literature. The globular mass may be confused with an enlarged inguinal node or a femoral hernia. Aspiration of seromucous fluid will differentiate it from the former, and pulsation on top of the tumor will distinguish it from the latter. A psoas abscess is more fluctuant. Unilateral chronic disease of the hip joint on the involved side suggests a possible associated bursitis. The simplest method of treatment is aspiration followed by administration of sclerosing solutions. If suppuration occurs, incision and packing are advocated.

Pusitz<sup>112</sup> believes that serious gunshot wounds of the hip and buttock with much fragmentation of the head, seen late, are best treated by resection of the femoral head, sulfonamide compounds and Orr's treatment. A reconstruction or arthrodesis may be performed subsequent to the control of the infection. In cases in which there is much destruction of tissue and in which a portion of

the sciatic nerve is lost, débridement removal of bone and, later, disarticulation of the hip may be indicated. One such case is reported in detail.

Watson and Berkman<sup>113</sup> state that failure to recognize march fractures of the femoral neck promptly may result in serious disability and deformity. They report the case of a soldier 34 years old who experienced sudden severe pain in his hip while hiking and a few days later had pain on the inner side of his thigh and knee. He continued activity, and one month later roentgenograms showed an incomplete fracture with shortening and limited motion of the hip. He was treated by traction for two weeks and then used crutches, without weight bearing, for four months.

Harmon and Adams<sup>114</sup> review the end results of surgical reconstruction in 53 patients who previously had had acute pyogenic arthritis. Chronically discharging sinuses responded satisfactorily to treatment in 80 per cent of the cases. Positional correction of an ankylosed hip, ankylosis of a painful hip and certain plastic procedures performed on young persons were found to be more satisfactory than arthroplastic procedures. Excision of the major part of the ilium in certain cases was thought to be of value when this portion of the pelvis was affected. Disarticulation of the hip joint should receive more consideration in the treatment of persistent suppuration of the hip joint in adults in the presence of osteomyelitis in the upper half of the femur. For young persons with unilateral instability of the hip joint the shelf operation is the procedure of choice, while for adults surgical arthrodesis is performed at the level of the acetabulum after the replacement of the dislocated hip. [Ed. NOTE (J. J. F.).—This article is well illustrated and many data are tabulated. Interested persons should refer to the original.]

Milch<sup>115</sup> is of the opinion that the angle of abduction is an unsatisfactory guide in performing an upper femoral osteotomy, and the postosteotomy angle is suggested instead. This angle represents the angle of the neck of the osteotomized femur and is measured by the line of the shaft and the line running from the upper end of the osteotomized shaft to the femoral neck.

113. Watson, F. C., and Berkman, E. F.: Fatigue (March) Fractures of Femoral Neck, *J. Bone & Joint Surg.* 26:404-405 (April) 1944.

114. Harmon, P. H., and Adams, C. O.: Pyogenic Coxitis: Indications for Surgical Treatment in Residual and Chronic Stages and End Results of Reconstruction in Fifty-Three Patients, *Surg., Gynec. & Obst.* 78:497-508 (May) 1944.

115. Milch, H.: The Postosteotomy Angle, *J. Bone & Joint Surg.* 26:394-400 (April) 1944.

110. Bergmann, E.: Role of Aseptic Bone Necrosis in Hip Lesions, *Am. J. Surg.* 63:218-235 (Feb.) 1944.

111. Stephens, V. R.: Tumor of Iliopectineal Bursa: Two Cases, *Arch. Surg.* 49:9-11 (July) 1944.

112. Pusitz, M. E., and Taylor, R. M.: Serious Gunshot Wounds of Hip, *J. Kansas M. Soc.* 44:397-400 (Dec.) 1943.

fractionation of human plasma. It is doubtful whether this source could ever fill the needs of surgeons except as a special material to be used sparingly by a few.

It is hoped that the gelatin sponge or foam may serve the same useful purposes as fibrin foam, as it can be produced in unlimited amounts from materials which are plentiful and cheap. This would make available to the entire membership of the surgical profession a new substance which can be of aid in controlling bleeding when other methods are not applicable.

sponge is apparently rapidly absorbed in the presence of an acute inflammatory reaction in which there is a dense polymorphonuclear leukocytic reaction. Foreign bodies of any type generally cause trouble in the presence of an acute inflammatory process, and it is of interest to know that gelatin sponge will undergo rapid "liquidation" in such circumstances. Thus may be avoided the development of a draining sinus down to the foreign material, which often occurs when the foreign substance is resistant to the action of leukocytes. On the other hand, if



Fig. 5.—Gelatin sponge in kidney after twenty-three days. The gelatin sponge has a thin zone of fibrous tissue at the peripheral portion, which invades the interstices. This zone of fibrous tissue separates the sponge from the kidney parenchyma, which was incised at this point and appears to have healed in, extruding the sponge from the incision. There are red cells in some interstices. Some macrophages have invaded the sponge, which is undergoing a moderate degree of absorption. Cellular response in the section is less than that about most foreign bodies such as surgical gut, linen or silk.

Sinclair and Douglas<sup>13</sup> found that the local implantation of gelatin into wounds leads to an accelerated fibroplasia and increased strength. In the light of these findings, it may be that the gelatin sponge supplies a substance locally which is beneficial to healing of the wound. Another point which should be brought out is that gelatin

there is no excessive leukocytic response to the sponge, it becomes incorporated in the tissues and gradually absorbed by a relatively mild phagocytic cell response.

The gelatin sponge has been used in 15 clinical cases in various ways to determine its behavior in human tissues. It has been used in



the fracture has solidly healed. The metal bar can then be removed and used again.

Clement<sup>130</sup> reports a study of 32 cases of march fracture in which the fracture was oblique in all early cases and the second and third metatarsal bones only were involved; these were longer than the first metatarsal bones in all but 2 cases, and the fracture line appeared on the medial surface in 29 cases. The increased length of the second and third metatarsal bones deranges the normal tripod structure of the foot, and march fracture results from stress and strain as a result of leverage on the bones, muscle pull of the lumbricalis and interosseus dorsalis muscles, which become spastic from irritation induced by marching.

Bosshardt<sup>131</sup> states that the high incidence of march fracture in German and Swiss armies is due to rigid cadence of marching. There is a definite difference between the occurrence in these two armies and that in the French army, which has an easy marching rhythm. American soldiers generally have led sedentary lives and have poor muscle tone and are therefore liable to have march fracture. The author believes that the fracture is primary and is related to a preexisting static disturbance of the foot, on which rhythmically repeated subthreshold mechanical insults have been acting. The treatment consists in rest and in physical therapy which incorporates exercises especially for dorsal and plantar flexion at the metatarsophalangeal joints.

Salmon's<sup>132</sup> report is based on 5 cases of march fracture. He relates that the absence of a history of direct trauma is responsible for some missed diagnoses. The characteristic appearances of the bone changes in the roentgenograms are described. Immobilization and rest are the suggested therapeutic measures.

Hullinger and Tyler<sup>133</sup> report 313 cases of march fracture in recruits undergoing training. The series includes a small number of cases of stress fractures in bones other than the metatarsals. It is believed that in 100 additional cases there were early march fractures which were completed by a definite trauma, but these cases have not been included in the series. A

detailed statistical analysis is made of the possible relationship of age, weight and other factors to the causation of the condition. The most interesting conclusion is that there is no predisposition to march fracture by any anatomic defect or variation, either acquired or congenital. The roentgenograms in the present series have been compared with three hundred roentgenograms of feet chosen at random. Measurements were taken of metatarsal length, width and spacing; position and conformity of sesamoid bones; length and width of feet, and general formation of foot. "There was no essential difference in the average of measurements in the two groups."

The general conclusion is that march fractures are brought about by trauma in the form of repeated subthreshold insults to the bone caused by walking. The determining factor is essentially a physiologic weakness secondary to fatigue. The incidence of march fractures is directly related to the severity of the training program. A new training order increasing the load carried by a man and the amount of exercise taken immediately resulted in a sharp increase in the number of patients with march fractures admitted to the hospital. The authors favor treatment by immobilization in a light walking plaster cast. They believe that if the bone is not protected from strain in this way callus will be excessive and recovery delayed. With treatment as outlined, all but 2 of the subjects returned to the full rigorous training program in an average of thirty-three days from the time of diagnosis.

[ED. NOTE.—The incidence of march fracture has increased because of the war so that it dominates the literature on the foot. The various reports seem to be in accord with regard to the history, symptoms and findings. There is some variation with regard to causation, but most authors feel that the change in the bone is a matter of strain and that there is an imbalance between the capacity of the bony structure and the demand made on these structures. The result is a disturbance which leads to the hypertrophic changes and the actual fracture. The treatment varies somewhat, although the consensus seems to be that more protection is needed, particularly in the acute phase. The rehabilitation of the foot to gain maximum capacity, so that the patient can carry out the duties of a soldier as soon as possible, is also stressed. This can be accomplished by means of walking casts or by means of a new device, a longitudinal steel bar in the shoe. This seems to fulfil the prerequisites of protection of the metatarsal bone and early resumption of activity.]

130. Clement, B. L.: March Fracture: A Common Disability of the Foot, *J. Bone & Joint Surg.* 26:148-150 (Jan.) 1944.

131. Bosshardt, C. E.: March Fracture: A Common Disability of the Foot in Military Practice, *Arch. Phys. Therapy* 25:41-44 (Jan.) 1944.

132. Salmon, J. K.: March Fracture, *J. Roy. Nav. M. Serv.* 30:1-5 (Jan.) 1944.

133. Hullinger, C. W., and Tyler, W. L.: March Fracture: Report of Three Hundred and Thirteen Cases *Bull. U. S. Army M. Dept.*, September 1944, no. 80, pp. 72-80.

this hemostatic substance. Bleeding from tooth sockets can be controlled by gelatin sponge.

The most hopeful use for the gelatin sponge might be as a first aid measure in military combat to pack into bleeding wounds when facilities are not available for the immediate treatment of the wounds. The use of a penicillin solution to moisten the sponge may have sufficient merit that it will be possible to control bleeding as well as infection until the patient is evacuated to a point where facilities permit more adequate care.

There is one point about gelatin sponge which must be considered, the fact that gelatin per se is an extremely good culture medium for bacteria and the introduction into contaminated wounds of a substance which would aid the growth of bacteria would not be without its limitations. It must be considered also that it is desirable to avoid or minimize the use of foreign material in a wound if possible. However, if one has the possibility of a troublesome hematoma to consider, there is justification for utilizing a substance which appears to present fewer hazards to the healing of the wound than a large hematoma.

#### SUMMARY

1. Gelatin sponge or foam was found to be a relatively bland substance which usually undergoes absorption by the phagocytic action of macrophages over a period of about five weeks.

2. The presence of a conspicuous number of polymorphonuclear leukocytes would generally lead to rapid absorption of the sponge within a few days to a week, by a liquefaction process.

3. The magnitude of the tissue reaction to the gelatin sponge during the period of absorption was generally less than that observed for surgical gut.

4. Gelatin sponge has a definite hemostatic action per se when applied to bleeding surfaces with moderate pressure.

#### CONCLUSIONS

Gelatin sponge or foam appears to have properties which make it suitable as an absorbable hemostatic substance and deserves clinical trial in the varied fields of surgery to further evaluate its merits and limitations.

foot in full dorsiflexion. A cast was worn two weeks, and roentgen ray check-up showed a normal left ankle. On this day the cast was removed and weight bearing allowed. In four days the swelling was no longer present, and good motion of the joint was present without pain or stiffness. The patient was discharged on full duty in approximately four weeks after the injury.

Braun<sup>149</sup> expresses great satisfaction in the results he obtained by conservative therapy for bilateral acquired pes cavus deformities of severe degree in a 24 year old seaman. The treatment consisted in manual stretching of the contractures, restoration of the articular function by manipulation, fulcral felt blockings and strapings, physical therapy and an appliance to establish proper balance of the feet with weight bearing. He states that this case demonstrates what success can be obtained by an intelligent approach to this condition.

Boyd<sup>150</sup> reports 4 additional cases of talonavicular synostosis, the patients being a white girl of 10 years, a white boy of 10 years, the boy's father aged 45 and the boy's grandmother aged 72. The relationships of the last 3 patients suggest a hereditary nature of the condition.

Cohen<sup>151</sup> reports an additional case (20 previous cases have been reported in the literature\*) of osteochondritis dissecans of the astragalus. An operation two weeks after the trauma afforded an opportunity to note capsular damage (ecchymosis) which may account for this lesion. Necrosis was rapid and probably occurred immediately after the vascular damage or, at most, within several weeks. A description of the observations at operation for the removal of the osteochondritic body, the microscopic pathologic changes and the differential diagnostic points between an osteochondritic body and a post-traumatic osteochondral fracture are presented.

Croce and Carpenter<sup>152</sup> state that tearing of the plantaris tendon or tennis leg occurs most frequently in middle-aged persons. The syndrome does not cause much disability and has not been widely investigated. The immediate cause of this syndrome and the end result are not definitely known. The authors present a case history which is unusual for three reasons:

1. The cause was direct trauma.
2. The tear

occurred near the origin of the muscle belly.

3. The injury resulted in a degenerative tumor of the muscle. It would seem that the plantaris tendon was torn from its origin along the linea aspera and probably deprived of its blood supply and a degenerative reaction of the belly of the muscle resulted.

Bickel and Moe<sup>153</sup> have described an operative procedure for the relief of paralytic calcaneal deformity of the foot resulting from poliomyelitis in 13 patients. The method consists in translocating the peroneus longus tendon by sliding it intact around the lateral border of the heel into a groove in the midline of the os calcis in an attempt to improve on the results obtained when the peroneal tendon is cut and transplanted into the tendo Achillis. They concluded that the best results were obtained when the operation was done on patients who had slight remaining power in the gastrocnemius muscles and fair or better power in the transposed peroneal muscle. It was their opinion that the results were strikingly better than if the peroneal tendon had been cut and then transplanted into the tendo Achillis.

A case of hereditary malformations of the hands and feet has been traced through four generations by Stiles and Pickard.<sup>154</sup> The defects in the extremities ranged from gross splitting of the hand or the foot to slight abnormalities of the digitis. An inspection of the pedigree reveals that the trait may be inherited as a single dominant. Modifying genes, environmental factors or a combination of both may be responsible for the extreme polymorphism of the character.

Experimental fractures in rabbits were treated by Blum<sup>155</sup> with phosphatase and calcium glycerophosphate with and without an anchoring medium (an alginate gel) employed to prevent the too rapid diffusion of the introduced enzyme from the region of the bone gap. Enzyme and substrate were either injected into the gel, which had been pressed into the bone gap, or were injected into the bone gap, in which the gel was subsequently formed in situ. Progress of repair of the bone was followed by roentgenograms and by histologic examination. The treated fractures showed acceleration of repair as compared with untreated controls.

149. Braun, G. S.: Bilateral Pes Cavus: A Case Report, U. S. Nav. M. Bull. 43:346-348 (Aug.) 1944.

150. Boyd, B. H.: Congenital Talonavicular Synostosis, J. Bone & Joint Surg. 26:682-686 (Oct.) 1944.

151. Cohen, H. H.: Osteochondritis Dissecans of the Astragalus, Bull. Hosp. Joint Dis. 4:86-91 (Oct.) 1943.

152. Croce, E. J., and Carpenter, G. K.: Rupture of the Plantaris Muscle, J. Bone & Joint Surg. 26:818-820 (Oct.) 1944.

153. Bickel, W. H., and Moe, J. H.: Translocation of the Peroneus Longus Tendon for Paralytic Calcaneus Deformity of the Foot, Surg., Gynec. & Obst. 78:627-630 (June) 1944.

154. Stiles, K. A., and Pickard, I. S.: Hereditary Malformations of the Hands and Feet, J. Hered. 34:341-344 (Nov.) 1943.

155. Blum, G.: Phosphatase and the Repair of Fractures, Lancet 2:75-78 (July 15) 1944.

epidermal changes were "nutritional and non-malignant," resulting from filling of the corium and subcutaneous tissue lymphatics with cancer cells originating in the deeper ducts or acini.

In 1900 Darier<sup>4</sup> considered the characteristic Paget changes as due to "dyskeratosis." This view has since found a considerable following. According to Darier, dyskeratosis consists in developmental segregation in the epidermis of a number of malpighian cells, which subsequently develop in an abnormal manner, independent of their fellows. In this group of dyskeratoses he included Bowen's disease, dyskeratosis follicularis, Paget's disease and molluscum contagiosum.

Jacobaeus<sup>9</sup> in 1904 originated the view that the so-called Paget cell is from the first a malignant cell and that it represents an extension into the epidermis from underlying glandular carcinoma. Cheate in 1923 and in 1930<sup>10</sup> concluded that changes in the epidermis might result from carcinoma originating in different foci and that the origin must be determined separately in each case.

In 1927 Sir Robert Muir<sup>11</sup> further elaborated the view of Jacobaeus. Through his studies Muir was able to demonstrate that in his material "Paget's disease" was consistently associated with changes in the ducts. These changes varied from hyperplasia to intraductal types of carcinoma. He defined a "Paget cell" as a mammary cancer cell growing within a non-neoplastic epidermis.

#### CLINICAL CHARACTERISTICS

What has been called "Paget's disease of the breast" begins as an intractable eczema of the nipple or areola (fig. 1). The patient's first recollection of the onset is an often recurring pruritis of the skin in this region. Again, the first symptom may be a simple crust associated with weeping or even bleeding of a minor character when it is removed. In some instances the first bleeding is noted to come from the summit of the nipple, though this may not correspond with the center of the cutaneous lesion. In any event the cutaneous lesion fails to respond to treatment with simple ointments or protection from irritating clothing and often alternates for long periods between weeping and drying with crust formation.

9. Jacobaeus, H. C.: Paget's Disease und sein Verhältniss zum Milchdrüsenkarzinom, Virchows Arch. f. path. Anat. 178:124, 1904.

10. Cheate, G. L., and Cutler, M.: Tumors of the Breast, Philadelphia, J. B. Lippincott Company, 1930.

11. Muir, R.: Paget's Disease of the Nipple and Its Relationships, J. Path. & Bact. 30:451-471 (April) 1927.

The ages of the patients studied in this series varied, but all patients were past 30. There was no decade which had a preponderance of the cases, though 22 of the 29 patients were

TABLE 1.—Age Distribution of Patients

Age Periods, Yr.*	Number of Cases
31 to 40.....	3
41 to 50.....	7
51 to 60.....	8
61 to 70.....	7
71 to 75†.....	4

\* The youngest patient was 31 years.

† The oldest patient was 75 years.

between 40 and 70 years when first seen. The duration of the cutaneous lesion before the patient consulted a physician varied within broad limits (table 2), but the preponderance of the

TABLE 2.—Duration of Cutaneous Lesion

	Cases, No.
Less than one month.....	3
One month to one year.....	12
One year to two years.....	6
Two years to three years.....	3
Three years to four years.....	2
Forty years.....	1
Thirty-five years.....	1
Unknown duration.....	1

patients here observed had noted a lesion on the skin for from one to three years previously. Three of the patients had noted a cutaneous manifestation for two weeks, thirty-five years and forty years respectively. The cutaneous lesion when ulcerated is usually bright red and inflamed, with a velvety surface of fine granular material. This may be small, or it may be extensive, with complete destruction of the nipple and involvement of the entire areola and contiguous cutaneous surface.

The patients in some instances complain also of a lump in the breast, though frequently one

TABLE 3.—Mass Palpable in Breast Affected

	Cases, No.	Cases, %
Yes.....	17	59
No.....	12	41

may be discovered which has escaped the notice of the patient. In this series 17 patients (59 per cent) presented a demonstrable breast mass while 12 (41 per cent) had no grossly evident mass (table 3). Clinically, any eczema of the breast should arouse suspicion, and any such lesion which does not completely respond in a period of two weeks to conservative therapy with a

the body and the tail of the pancreas develop. Diverse views are still entertained concerning the duplicity of the ventral anlage, which arises in close proximity to the common duct. Some maintain that the bud is single, while others

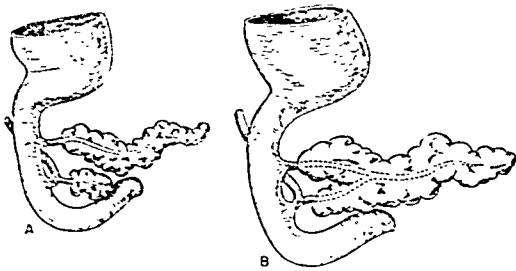


Fig. 1.—Pancreas of a human embryo: *A*, fifth week; *B*, seventh week.

rounded by pancreatic tissue; pancreatic tissue may occur even in the wall of the duct itself.

This relation of the exact point of origin of the persisting ventral bud to the common duct determines the final relation of the main pancreatic duct to the common duct. If the pancreatic anlage has grown out from the wall of the common duct itself, the final pancreatic duct will open into the ampulla of the common duct. If the pancreatic anlage has grown out from the wall of the common duct itself, the final pancreatic duct will open into the ampulla of the common duct. If the pancreatic anlage has grown out from the wall of the gut in close proximity to the common duct, the openings of the two ducts will be in close proximity, yet the

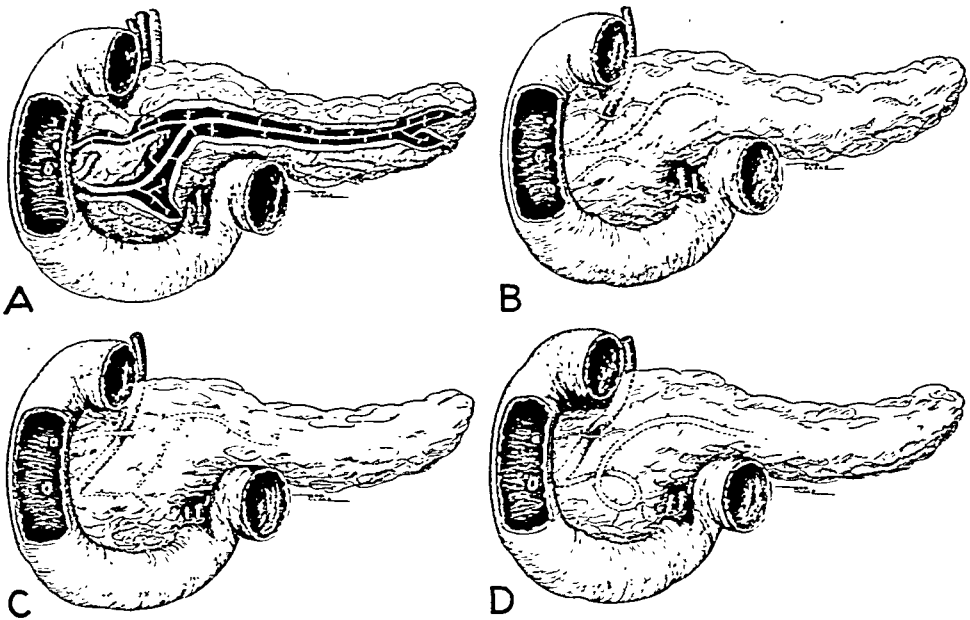


Fig. 2.—*A*, the most constant arrangement of the pancreatic ducts; *B*, specimen with three papillae; *C*, dissected specimen of an adult pancreas showing an embryonic type of duct system in which the accessory duct carries most of the pancreatic secretion; *D*, dissected specimen of an adult pancreas showing an unusual loop configuration of the main pancreatic duct.

old that at the beginning it consists of two lateral halves which subsequently fuse or one of which disappears, perhaps forming the source of aberrant pancreatic tissue often found along the wall of the gut. As development progresses, the ducts unite, as shown in figure 1 *B*, the duct of the dorsal anlage undergoing a certain degree of atrophy at its duodenal end<sup>11</sup> to produce the adult arrangement, shown in figure 2 *A*.

The close relationship between this portion of the pancreas and the common duct is thereby explained. Depending on the eccentricities of development, the relationship will vary somewhat: the common duct may be entirely sur-

rounded by pancreatic tissue; pancreatic tissue may really open into the intestine and not into the ampulla at all.

The facts seem to be these: Both buds develop by growth in continuity, the dorsal bud giving origin to all of the gland except that portion of the head in close proximity to the common duct and the intestinal wall. The persisting ventral bud grows out but a little way and then fuses with the dorsal bud, giving origin to but a small part of the glandular tissue of the caudal part of the head of the pancreas. In the majority of cases the duct system of this ventral anlage becomes the more important duct system from the point of fusion of the two anlages to the wall of the gut (fig. 1 *B*).

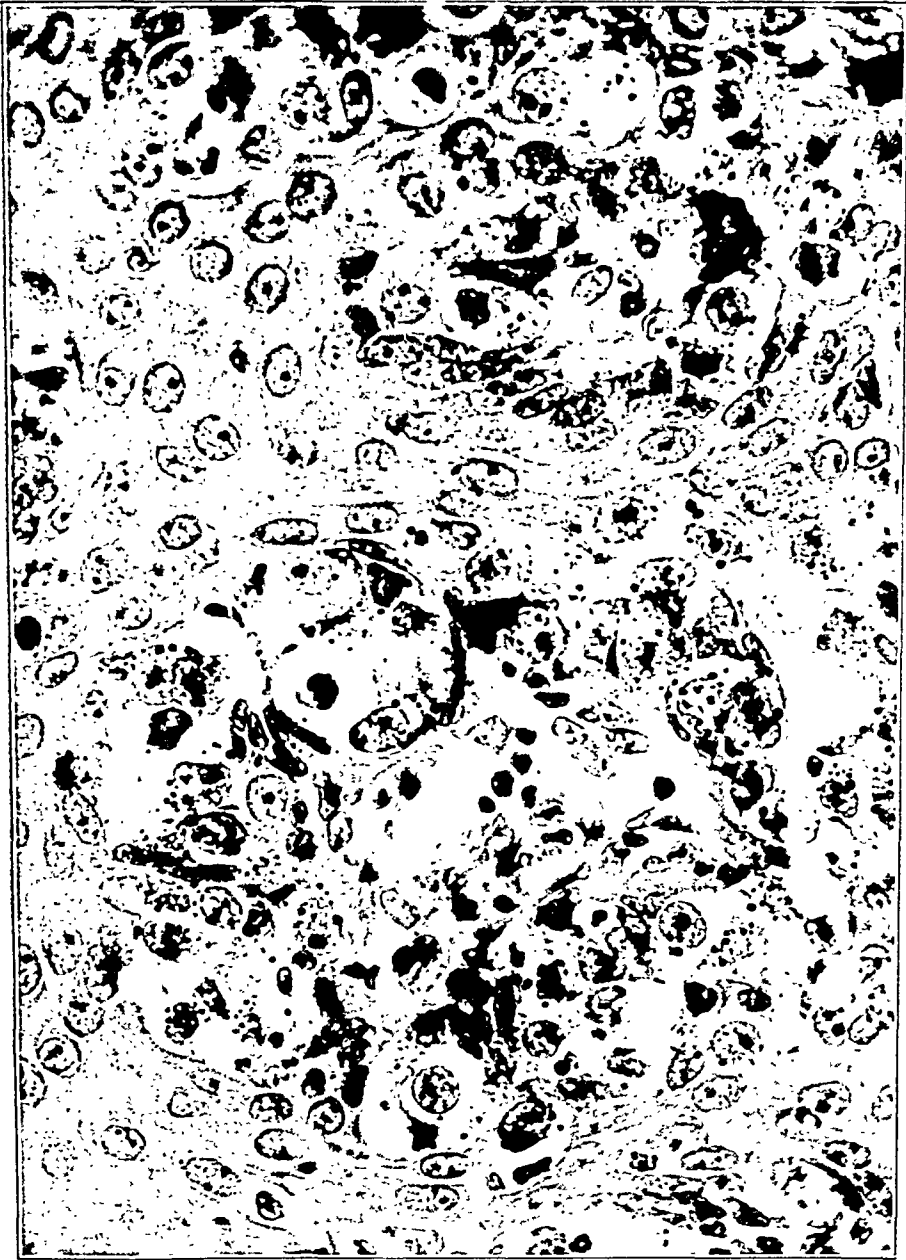


Fig. 2.—A view of the epidermis from a case such as that seen under lower magnification in figure 1 ("Paget's disease"). Here one sees the intraepidermal malignant cells dispersed singly and in bizarre clusters among the epidermal cells. Note that the neoplastic cells ("Paget cells") are generally large and have clear cytoplasm and pyknotic nuclei, and in no instance can be demonstrated intercellular bridges between the abnormal cells and the epidermal cells. The latter characteristic is in favor of the theory that the abnormal cells do not arise in the epidermis. Note also, in this regard, that the contiguous epidermal cells are displaced and compressed by the growth of the neoplastic cells ( $\times 400$ ).

Schieffer<sup>28</sup> on human fetuses and still later by Baldwin,<sup>29</sup> who made microscopic preparations of the terminal part of the accessory duct and the minor papilla.

The average diameter of the undistended duct in the 85 specimens with a normal duct arrangement at its point of perforation of the duodenal wall was 1.6 mm. The size of the duct, however, was no criterion of its patency, for only 62, about 73 per cent, were found to be patent by use of the injection method, whereby either air or dyes or both were injected under minimal pressure in order to avoid breaking through any natural barrier which might have been present. This gives, then, 23 specimens, about 27 per cent, which did not communicate with the duodenum. This is considerably higher than Helly's 20 per cent<sup>31</sup> and Baldwin's 10 per cent of 50 specimens,<sup>26</sup> in both groups of which the terminal part of the accessory duct was examined microscopically. These results, however, are in accord with those obtained by use of the injection technique (see table 2).

TABLE 2.—Patency of the Accessory Duct

	Injection Method	
	Patent	Closed
Schirmer.....	85	19
Charpy.....	9	21
Oplie.....	79	21
Verneuil.....	20	0
Sappey.....	16	1
Rienhoff and Pickrell.....	62	23
Total.....	271	85
Per cent.....	76	24

In the 4 instances in which the duct system was reversed and the 11 instances in which no intraglandular communication of the ducts could be demonstrated, the accessory duct approached the duodenum with increasing caliber and with a patent papilla, leaving 23 per cent of all specimens in which the papilla was closed, regardless of the duct arrangement. Of practical interest, however, is the fact that in 11 per cent the ducts did not communicate and in 23 per cent the papilla was closed, making a total of 34 per cent in which fluid could not pass from the main duct to the duodenum by way of the accessory duct.

Complete absence of the accessory duct seems to be a rare anomaly, since it occurs in less than 1 per cent of specimens examined (table 3). Inversion of the ducts occurs in about 7 per cent (table 4).

28. Schieffer, J.: Du pancreas dans la série animale, Thesis, Montpellier, 1884.

#### RELATION OF THE AMPULLA OF VATER TO PANCREATITIS

Bécourt,<sup>29</sup> Bernard<sup>12</sup> and Laguesse<sup>30</sup> each mentioned 1 specimen in which the main pancreatic duct opened into the duodenum apart from the orifice of the bile duct. Schirmer<sup>5</sup> found 22 specimens, about 47 per cent, among 47 investigated in which a mucosal septum separated the orifice in such a manner that a true ampulla did not exist. Practically all textbooks of anatomy<sup>24</sup> describe the ducts as usually uniting to form a common channel at their duodenal extremities. Sappey<sup>25</sup> stated that this arrangement is the one which is observed in the great

TABLE 3.—The Accessory Duct

	Present	Absent
Schirmer.....	101	3
Charpy.....	29	1
Helly.....	50	0
Verneuil.....	20	0
Santorini.....	?	0
Bernard.....	?	0
Hamburger.....	50+	0
Sappey.....	17	0
Oplie.....	100	0
Baldwin.....	76	0
Rienhoff and Pickrell.....	100	0
Total.....	543	4
Per cent.....		0.737

TABLE 4.—Inversion of Ducts

	Specimens Examined	Inversion of Ducts
Schirmer.....	104	4
Charpy.....	20	3
Bernard.....	?	1
Morel and Duval.....	?	1
Oplie.....	100	11
Elmar.....	?	1
Moyse.....	?	1
Baldwin.....	76	3
Rienhoff and Pickrell.....	100	4
Total.....	410	29
Per cent.....		6.61

majority of cases. One of few exceptions to this view is found in the frequently cited work of Letulle and Nattan-Larrier,<sup>18a</sup> who found that a common channel occurred in only 8, about 38 per cent, of 21 specimens.

Schirmer<sup>5</sup> mentioned 11 specimens in his series of 47 in which the pancreatic duct opened into the bile duct and 14 specimens in the same series in which the bile duct opened into the pancreatic duct. Verneuil<sup>31</sup> seemed to believe

29. Bécourt, P. J. G.: Recherches sur le pancréas, Strasbourg, F. G. Levrault, 1830.

30. Laguesse, E.: Sur l'existence de nouveaux bourgeons pancréatiques accessoires tardifs, *Compt. rend. Soc. de biol.* 2:602, 1895.

31. Verneuil, A.: Mémoire sur quelques points de l'anatomie du pancréas, *Gaz. méd. de Paris* 6:384 and 398, 1851; reprint ed., Paris, E. Thunot & Cie, 1851.

lastic cell, the so-called Paget cell. This cell varies in size and other characteristics, just as any neoplastic cell might in any other locus. It is usually round or ovoid. Its nucleus is hyperchromatic, and mitotic figures are occasionally

degeneration (fig. 2). Characteristically, this neoplastic cell is surrounded by a clear space, and in no instance are intercellular bridges found to exist between it and the prickle cells. This picture must be differentiated from (1) Bowen's

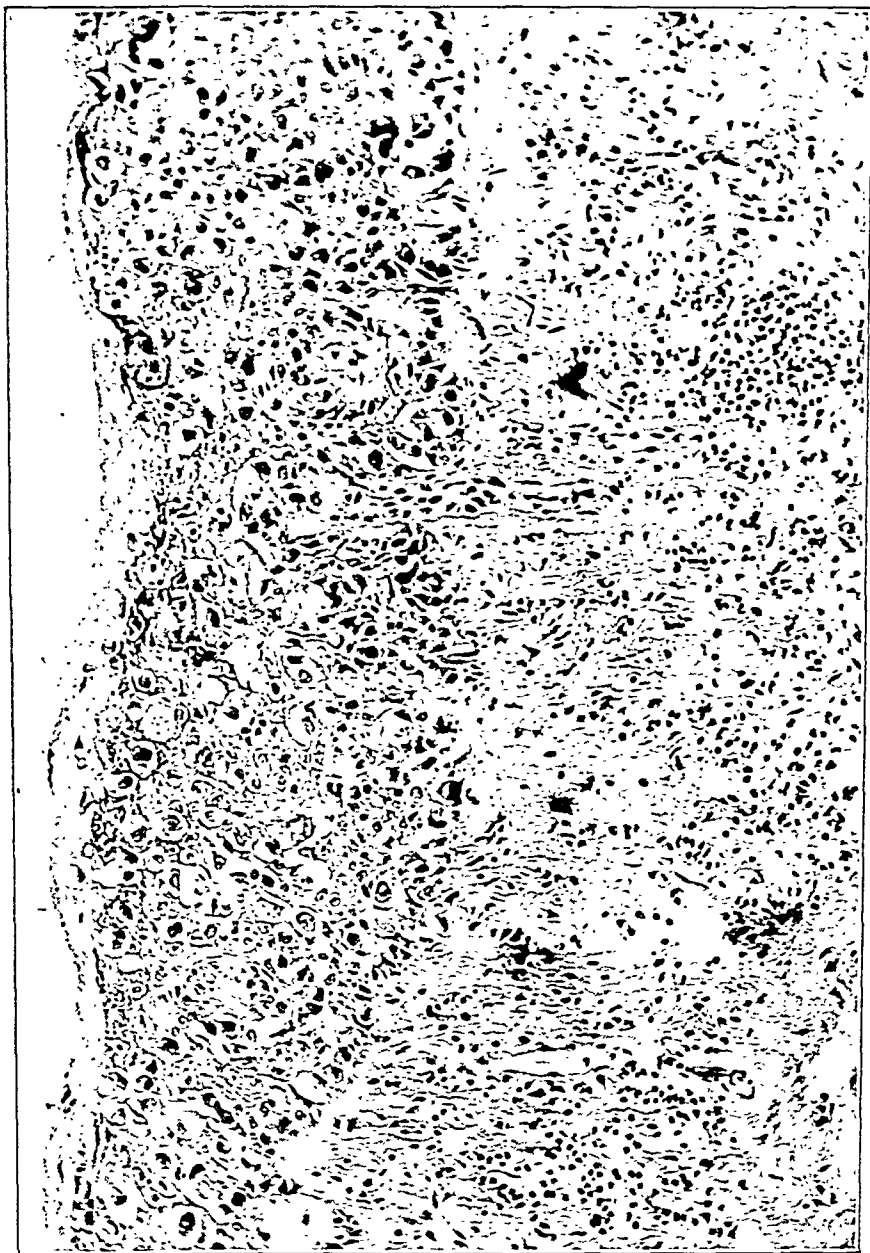


Fig. 4.—Bowen's disease of the skin. Here, again, the characteristic feature of the microscopic picture is the presence in the epidermis of abnormal cells. The Bowen cells, though large, have much intracellular edema and eccentrically located nuclei. Multinucleated cells are common and are spoken of as "basket cells." Hyperkeratosis as seen here is a frequent accompaniment of this lesion, while it is absent in intraepidermal metastasis ("Paget's disease") ( $\times 140$ ).

seen (fig. 3). The cells may occur singly or in bizarre clusters. The adjacent epidermal cells are often distorted by compression or hydropic

disease. (2) superficial epitheliomatosis, (3) simple eczema of the nipple and (4) squamous cell carcinoma of the breast.



the majority of instances, then, a calculus must be 4 mm. in diameter before it can cause obstruction, if one assumes that it is approximately spherical. This, however, seems the exception rather than the rule, since irregularly shaped calculi are encountered more frequently than spherical ones. This leaves, then, 47 specimens, about 18 per cent, in which the length of the ampulla exceeded the average diameter of the duodenal orifice and in which a complete block at the papilla by an impacted calculus would convert the ducts into a communicating system. This reasoning, however, is open to several serious objections. In the first place, conclusions formulated from measurements taken between poorly defined points, of differences of 1 mm. or less, seem decidedly inaccurate, since average measurements may never actually occur in a single instance. In the second place, the obstructing calculus was spherical, when irregularly shaped calculi are encountered more frequently, and, as suggested by Cameron and Noble,<sup>42</sup> a considerable part of an irregularly shaped calculus may project through the orifice of the ampulla into the duodenum, while its length may exceed that of the ampulla, and yet a reflux would be possible. It is true, also, that the greatest diameter of an impacted calculus may equal the long diameter of the ampulla in which it is wholly contained, with a communication existing between the ducts owing to the failure of the irregularly shaped calculus to completely fill the ampulla, which itself may be dilated.

Although it is a matter of definition as to whether an ampulla actually exists in those instances in which the septum extends within 2 mm. of the apex of the papilla, in table 6, in

TABLE 6.—*The Ampulla of Vater*

	Ducts Join to Form Ampulla	No Junction	Specimens Examined
Bécourt.....	?	1	?
Bernard.....	?	1	?
Laguesse.....	?	1	?
Schirmer.....	25	22	47
Letulle.....	8	13	21
Opie.....	89	11	100
Ruge.....	32	11	43
Baldwin.....	56	34	90
Belou.....	8	42	50
Mann and Giordano.....	40	169	209
Cameron and Noble.....	74	26	100
Rienhoff and Pickrell....	51	169	250
Total.....	413	491	901
Per cent.....	46	53	

which the measurements are given a true ampulla was not considered present in the specimens. From the figures in table 6, we see that

an ampulla is present in about 46 per cent, had the measurements been included in each investigator's report. For example, Cameron and Noble made no mention of the ampullae less than 5 mm., while in Opie's series of 100 specimens, in only 30 did this measurement equal or exceed 5 mm. Oser found only 32 of 100 specimens in which the diverticulum was of such size that a small calculus might occlude the orifice without completely filling it and thus obstruct both ducts. Our findings and the correlation of the greater part of the work done on this particular phase of the problem to the present time lead us to believe that the main pancreatic duct enters the duodenum apart from the common bile duct in 25 to 30 per cent of all cases and that a true ampulla is present in only 30 to 40 per cent.

#### THE RELATION OF THE SPHINCTER OF ODDI TO PANCREATITIS

Although Glisson<sup>45</sup> expressed the opinion that a sphincter existed at the end of the common bile duct, it was first described by Gage,<sup>46</sup> who studied the sphincter in the cat and found sphincters around the pancreatic and common bile ducts and one group of muscle fibers passing around both ducts. Oddi,<sup>47</sup> employing many species of animals, made an extensive comparative anatomic and physiologic study of the sphincter; but, aside from assigning a special sphincter to the duct of Wirsung, he did not study especially the relation of the sphincter of the common bile duct to the pancreatic duct. Somewhat later, Hendrickson<sup>48</sup> studied the sphincter in man, in the dog and in the rabbit. His specimens show muscle fibers surrounding both the common bile and the pancreatic duct.

In the absence of a stone in the ampulla of Vater, it has been suggested that in the instances in which both the bile and pancreatic duct open together in the ampulla, a flow of bile from the common duct might be diverted into the pancreatic duct during life by spasm of the sphincter of Oddi.

The possible importance of the sphincter at the duodenal end of the common bile duct was

45. Glisson, quoted by Oddi.<sup>47a</sup>

46. Gage, S. H.: The Ampulla of Vater and the Pancreatic Ducts in the Domestic Cat, *Am. Quart. Micr. J.* 1:123 and 169, 1878-1879 (pl. xii-xiv).

47. Oddi, R.: (a) D'une disposition à sphincter spéciale de l'ouverture du canal cholédoque, *Arch. ital. de biol.* 8:317, 1887; (b) Sulla tonicità dello sfintere del coledoco, *Arch. per le sc. med.* 12:333, 1888.

48. Hendrickson, W. F.: A Study of the Musculature of the Entire Extrahepatic Biliary System, *Bull. Johns Hopkins Hosp.* 9:221, 1898.

TABLE 4.—Summary of Data in 29 Cases of Cancer of the Breast

Case No.	Age, Yr.	Duration of Cutaneous Lesion	Palpable Mass	Clinical Picture	Pathology	Course
1	45	2 yr.	Yes	Two years ago patient taped both nipples with adhesive tape; right nipple became irritated and has refused to heal; nipple discolored serum and has been seat of constant pruritus; lump present in right breast many years Examination: Right nipple denuded, with raw, moist, bleeding surface; 2 in. (5 cm.) above right nipple is indurated 1 in. (2.5 cm.) nodule; no nodes palpable	Adenocarcinoma of breast, with continuity of carcinoma cells in dermis into epidermis; in addition to intraepidermal extensions, ulceration and chronic inflammatory reaction found	Cutaneous lesion treated with petrolatum dressing for 6 wks. with no improvement; 10/6/29, radical mastectomy performed; 8/22/31, no recurrence demonstrable
2	56	?	No	Patient's mother had carcinoma of the breast; patient responded by kitten; pruritic and bleeding lesion ensued; no response to treatment with ointment; 40 per cent areola ulcerated and crusted; no nodes palpable	Intraductal carcinoma and intraepidermal malignant cells (Paget); no metastases to lymph nodes	Biopsy of nipple revealed "Paget's disease"; 11/29/34, radical mastectomy performed; 9/15/44, no recurrence demonstrable
3	51	3 wk.	Yes	Patient aware of lump in left breast for 30 yr.; 3 wk. ago small ulcer developed at dome of left nipple, with no bleeding from lesion or nipple; nipple is verrucous, with crusted, 8 cm. ulcer; palpable mass deep in outer lower quadrant, which is not attached to the skin	Adenocarcinoma of breast and intraepidermal metastases (Paget's disease of the skin)	10/29/37, simple mastectomy performed, physician believing patient had "cystic disease and keratosis of nipple"; 12/3/37, radical excision of residual completed; 11/22/41, no recurrence found
4	61	1 yr.	No	Patient noted crusted lesion at tip of left nipple for 1 yr.; "gradually becoming worse" Examination: Reveals such a lesion measuring 4 sq. cm.	(1) Typical "Paget's disease of nipple"; (2) adenocarcinoma of breast, with extensive axillary metastases	(1) 7/20/37, lesion and entire nipple excised; 3/18/38, 3 cm. hard mass in scar and 1 cm. soft nodule in left axilla discovered; (2) 1/1/38, radical mastectomy performed on left side; 11/11/40, patient died from generalized carcinomatosis
5	70	3 yr.	No	For 3 yr. patient had pruritus and burning of right nipple, also ulceration of nipple, with periods of healing Examination: Nipple eroded away by 6 cm. ulcer; no nodes palpable	Intraductal carcinoma; duct lined with malignant cells extends to skin of nipple and becomes continuous with intraepidermal invasion by malignant "Paget" cells	Simple mastectomy performed (because of patient's age) 7/12/33; 3/17/33, no recurrence
6	61	1 yr.	Yes	One year ago patient observed skin of left nipple "peeling off"; this continued, with no pain or discharge Examination: 2 cm. soft, pink excoriated left nipple; deep in breast tissue in upper outer quadrant is 3 by 1 cm. irregular mass	Biopsy reveals typical intraepidermal malignant cells, with intact basal cell layer; ductal carcinoma in underlying breast ducts	7/28/45, radical mastectomy performed on left side
7	40	0 mo.	Yes	Existing ulcer of left breast present for 6 mo. Examination: Superficial erosion of left nipple; subjacent to nipple is firm, hard mass fixed to the skin; hard, movable node palpable in left axilla	Adenocarcinoma of breast, and at epidermal margin, adenocarcinoma extensions; also in these zones are intraepidermal extensions of same cells, showing the typical picture of "Paget's disease"	8/11/44, radical mastectomy performed; 12/6/44, no evidence of recurrence
8	40	20 mo.	Yes	Patient discovered induration and pain around right nipple 20 mo. ago; some bloody discharge associated with this Examination: Half of nipple excoriated and granulating; hard fixed subjacent mass palpable in breast	Adenocarcinoma of breast in continuity with epidermal picture of "Paget's disease"; some extensions of malignant cells can be traced into epidermis, in which they appear as "Paget cells"—actually malignant cells	12/2/23, radical mastectomy performed; no recurrence found when patient was last seen, 1/19/40
9	40	5 mo.	Yes	Five months ago patient noted her clothing adhering to left nipple; crust formed, with occasional bloody discharge; small lump noted at same time, which has increased slightly in size Examination: 7 cm. crusted ulcer on left nipple; subjacent to it is 1 cm. mass; 1 cm. hard node palpable in left axilla	Adenocarcinoma of breast with lymph node metastases; nipple lesion presents typical picture described as "Paget's disease," with resemblance of "Paget cells" to carcinoma cells of breast	8/9/40, radical mastectomy performed on left side; in 1942 patient died of hypertension
10	40	8 wk.	No	Eight weeks ago patient noted small red spot on left nipple; has had some pruritus	Adenocarcinoma of left breast and changes characteristic of "Paget's disease" in skin of nipple	12/20/40, simple mastectomy performed on left side; 12/20/42, no recurrence; patient not seen since

ie hemorrhage is the result of a vasomotor flux; others believe that it results from venous thrombosis, and still others believe that it results from the erosion of the blood vessels by the pancreatic trypsin. Rich and Duff<sup>2</sup> found that the specific vascular lesion causing the hemorrhage was located especially in the media of the vessel, where the muscle fibers are swollen, their nuclei pyknotic and often separated by fluid spaces. The adventitia may appear condensed and pink staining and contain polymorphonuclear leukocytes. The internal elastic membrane becomes frayed, loses its undulations and takes on a swollen appearance. The first alterations of the media are found in its outer layers, the muscle fibers of which become necrotic while those near the intima remain intact. But the process is apparently a rapid one and proceeds rapidly to involve the entire thickness of the vessel wall, with final destruction of the intima. Destruction of a segment of the vessel wall was found most frequently in the larger arteries, while destruction of the whole circumference was the rule in the smaller vessels. The lesion is quite indistinguishable from that characteristic of the familiar arteriolonecrosis and hyaline arteriosclerosis occurring in man in association with hypertension and in arteriosclerotic nephritis.

#### SUMMARY

The historical aspects concerning the anatomy of the pancreas have been reiterated. The embryology of the pancreatic systems has been reviewed. The etiologic factors of pancreatitis have been discussed.

The anomalies and their results encountered in 250 dissections of the pancreatic systems are tabulated and discussed with their clinical significance. In 73 instances, about 24 per cent, there could be found no junction of the pancreatic and bile ducts, each entering the duodenum with

separate orifices. In 92 instances, 37 per cent, the ducts were contiguous, the dividing septum terminating 1 to 2 mm. from the apex of their common orifice. In this group, however, a true ampulla was not considered present. In 81 instances, 32 per cent, a true ampulla was present, varying in length from 3 to 14 mm., while in 4 instances, 2 per cent, the main pancreatic duct was reduced to a fibrous cord.

In 47 instances, 18 per cent, the length of the ampulla exceeded the average diameter of the duodenal orifice, and a complete block at the papilla would convert the two ducts into a communicating system.

The average diameter of the duodenal papilla was 3 mm., with limits of 1.5 and 4.5 mm.

Concerning the accessory pancreatic duct, in only 89 of 100 specimens studied for this purpose could any intraglandular communication between the ducts be demonstrated. In 4 instances, the embryonic duct system was present—i. e., the accessory duct carried the greater part of the secretion—while the main duct was reduced to a fibrous cord, leaving 85 specimens with a normal duct arrangement. In only 62 of these, 73 per cent, was the duct found to be patent, or there were 23 instances in which the accessory duct did not communicate with the duodenum, regardless of the duct arrangement, making a total of 34 per cent in which fluid could not pass from the main pancreatic duct to the duodenum by way of the accessory duct. The average diameter of the undistended duct at its point of perforation of the duodenum was 1.6 mm.

The anatomic position and arrangement of the sphincter of Oddi and the conditions modifying its resistance are discussed, and the current theories postulated regarding the necrosis and hemorrhage which occur are briefly discussed.

TABLE 4.—Summary of Data in 29 Cases of Cancer of the Breast—Continued

Onset Yr.	Age, Yr.	Duration Cutaneous Lesion	Palpable Mass	Clinical Picture	Pathology	Course
21	31	2 yr.	No	Pruritus of right nipple present for 2 yr.; in recent months small, exuding ulcer of nipple developed, with occasional bleeding. Examination: Excoriation, with serous sanguinous weeping of nipple; no mass or palpable nodes discernible.	Intraductal carcinoma; in one focus can be seen invasion through wall of a duct; typical "Paget's disease of skin," with close resemblance of intra-epidermal and intraductal malignant cells.	9/7/11, radical mastectomy performed on left side; 1/30/15, no evidence of recurrence
22	69	18 mo.	No	For 18 mo. patient noted chapping and cracking of right nipple with pruritus; slow enlargement of lesion. Examination: 6 mm. superficial ulcer of right nipple, with induration of entire nipple; no palpable mass found; two small, movable nodes present in each axilla.	Adenocarcinoma with lymph node metastases; sections demonstrate nests of adenocarcinoma at basal cell layer of epidermis, with "Paget cells" in adjacent epidermis—identical with carcinoma cells; also lymphatics in derma containing carcinoma cells.	9/5/13, radical mastectomy performed on right side; 2/2/15, no recurrence found
23	59	3 yr.	Yes	Three years ago patient noted white film over right nipple, with a pinhead hole in its center; crust and discharge followed, and slowly nipple eroded away; 4 mo. ago patient noted mass in upper part of breast. Examination: 8 cm. mass, movable in upper part of breast; nipple is eroded away, with replacement by dirty ulcer.	In some sections are adenocarcinomatous arrangements in dermis extending to basal cell layer; in others is duct extension into epidermis; duct also seen, lined with malignant epithelium; these cells identical with intraepidermal malignant cells ("Paget")	5/1/11, simple mastectomy performed; 11/23/11, patient died at city sanatorium with a "pyothorax"
24	78	3 wk.	Yes	In 1909, patient had mastectomy and axillary dissection on right for carcinoma of breast; 10 mo. ago lump noted in left breast and left axilla; for 3 wk. soreness and crusting of left nipple noted. Examination: Left nipple enlarged, ulcerated and crusted; 5 cm. hard mass palpable in lower outer quadrant of left breast, and four hard nodes found in left axilla.	Breast adenocarcinoma and "Paget's disease of skin"	5/27/11, axillary dissection and radical mastectomy performed on left side; 7/30/11, lump in right axilla; 8/1/11, axillary dissection performed on right side
25	58	6 mo.	Yes	Small excoriation on right nipple noted 6 mo. before, which ulcerated with crusting and oozing serum; discharge from nipple for 2 mo. Examination: 3 by 4 cm. ulcer of right nipple, with sharp margins, seen; retraction of nipple pronounced.	Deep to the ulcer is 2 cm. mass containing ductal carcinoma; in one section is duct lined with malignant cells identical with "Paget's cells" seen in adjacent epidermis.	2/12/36, simple mastectomy performed on right side
26	32	2 yr.	Yes	Left radical mastectomy performed 10 yr. ago for carcinoma; white discharge from right nipple, with crusting of skin, present for 2 yr.; patient noted mass in right breast 2 wk. ago. Examination: Retracted right nipple, with white discharge and crusting of nipple skin; 2 cm. mass present in upper outer breast quadrant; it is not attached to the skin; hard mass palpable in right axilla.	An adenocarcinoma with axillary metastases; changes in skin typical of "Paget's disease"; in one section is duct filled with malignant cells, and at ampulla the continuity of extension of duct neoplasm with that of epidermis can be traced as they are seen to invade the epidermis at the margin of the ampulla epithelium.	7/7/33, radical mastectomy performed on right side; 11/21/41, small shot-sized node presented in right side of neck; intractable headaches, vomiting and progressive paralysis of right arm developed; 1/10/42, patient died
27	50	4 wk.	Yes	Small lump in each breast present for 4 wk. Examination: Each nipple retracted, with leathery mass adjacent to and attached to nipple.	Adenocarcinoma in each breast; in the skin is typical picture of "Paget's disease"; malignant cells found in the dermis, extending into the epidermis; also in epidermis are multiple epidermal cells in state of hyaline degeneration.	12/3/11, bilateral simple mastectomy performed; no follow-up
28	63	?	Yes	Mass in right breast noted 1 yr. ago; gradually increased to about three times its original size. Examination: Retraction of skin of nipple; an orange-colored mass in outer lower quadrant of right breast attached to skin.	Adenocarcinoma of breast with extension into all layers of skin and ulceration in one zone; in margins of ulcerated zone are two atypical cell types in epidermis; epidermal cells with hyaline degeneration and malignant cells identical with those in carcinoma of breast tissue; latter are characteristic "Paget cells"	10/27/31, right radical mastectomy performed; 3/5/32, patient died of undetermined cause
29	68	6 mo.	No	Eczema-like eruption around right nipple present 6 mo. and failed to heal or improve with applications of ointments	Ductal carcinoma of the breast found, and some ducts filled with carcinoma cells traced to the epidermis, in which was a typical intraepidermal metastasis (Paget's disease)	5/11/15, simple mastectomy performed

once to a little more than twice or even two and a half times the diameter of the red cells which pass through them. The red cells usually pass in single file or, at most, a double row. When a capillary contracts or is compressed to just a little less than the diameter of the contained red cells, the red cells rub on the inner surface of the endothelium and thus resist passage, and the flow through that vessel soon stops (see Krogh,<sup>14</sup> page 11, and Knisely<sup>15</sup>). Most true capillaries can dilate without losing tonus, weakening and sacculating to a little more, but usually not much more, than two or two and a half times the diameter of the contained red cells (Krogh,<sup>14</sup> p. 335, and Knisely, Stratman-Thomas, Eliot and Bloch<sup>6</sup>). The arterioles of most of the organs in frogs and mammals which we have studied are long, narrow, tapering cones. During the flow of blood through them, their outlet tips vary either anatomically or functionally from a little wider to a little narrower than the capillaries or sinusoids they join and supply. These statements are true of the arterioles and capillaries of the bulbar conjunctiva of human beings and almost certainly true of the arterioles and capillaries of many other human organs during life. Arteriovenous anastomoses have thus far been found in but a few organs of any one species. The arteriovenous anastomoses which have been found are often closed and when open are frequently but two or three times the diameter of the red cells passing through them (see the reviews by E. R. Clark<sup>15</sup> and Boyd<sup>16</sup>). These are key points for understanding some of the pathologic processes initiated by intravascular agglutination of the blood, for they show that most of the time, under most conditions, nearly all the circulating blood must pass through vessels having an internal diameter from about once to twice or at most three times that of the red cells on every trip from the left side of the heart through the circulatory system and return. Thus, as is well known but not always remembered, the arterioles and capillaries are a perpetual "bottleneck" in the vascular system.

*C. Some Changes in the Blood and Vessel Walls During Stage III of P. knowlesi Malaria.*—At the beginning of stage III of the pathologic circulatory physiology of rhesus monkeys with *P. knowlesi* malaria, a thick, glassy precipitate forms between and around all the blood cells of the animal. In this malaria, this

precipitate forms throughout all of the animal's circulatory system at one time. The process acts as though it were autocatalytic; once it starts, it usually goes on to completion in from ten to about twenty minutes. This precipitate binds the animal's red cells together in wads and masses (*not rouleaux*), which by microscopic standards are large, semirigid and tough, and thereby rapidly changes all the animal's circulating blood into a thick, mucklike sludge.

As soon as the blood has changed to this thick, pasty sludge, a definite sequence of events takes place. Three major steps are as follows:

1. This sludge resists its own passage through small vessels much more than does normally fluid blood; consequently, the rate of flow through small vessels all over the body becomes progressively slower than the normal rates for each degree of dilatation of each vessel. This increased resistance to flow and consequent reduced rates of flow through the capillary beds slowly, progressively and inescapably leads to various degrees of stagnant anoxia all over the body.

2. There is a time interval of variable length during which (a) the reduced rates of flow are unmistakable and (b) there is still no visible hemoconcentration of the sludge passing through peripheral vascular beds. During this period, the flow through each small vessel is slower than the normal rate for whatever degree it is dilated but the vessels have not yet begun to leak perceptibly (see the scenes following titles 29, 30 and 31 in the Knowlesi Malaria film<sup>7</sup>). After the sludged blood has been flowing too slowly for a time, the walls of postcapillary venules and small venules lose their ability to retain blood colloids. Anoxia of the endothelium is alone sufficient to cause this (see Starr<sup>17</sup>; Starling<sup>18</sup>; Landis<sup>19</sup>; Krogh,<sup>14</sup> pp. 321, 326 and 335; Maurer<sup>20</sup>; Warren and Drinker<sup>21</sup>; Drinker<sup>22</sup>

17. Starr, I., Jr.: Production of Albuminuria by Renal Vasoconstriction in Animals and Man. *J. Exper. Med.* **43**: 31 (Jan.) 1926.

18. Starling, E. H.: Principles of Human Physiology, ed. 4, Philadelphia, Lea & Febiger, 1926, p. 854.

19. Landis, E. M.: Micro-Injection Studies of Capillary Permeability: III. The Effect of Lack of Oxygen on the Permeability of the Capillary Wall to Fluid and to the Plasma Proteins, *Am. J. Physiol.* **83**: 528 (Jan.) 1928.

20. Maurer, F. W.: The Effects of Decreased Blood Oxygen and Increased Blood Carbon Dioxide on the Flow and Composition of Cervical and Cardiac Lymph. *Am. J. Physiol.* **131**: 331 (Dec.) 1940; The Effects of Carbon Monoxide Anoxemia on the Flow and Composition of Cervical Lymph, *ibid.* **133**: 170 (May) 1941; The Effects of Anoxemia Due to Carbon Monoxide

15. Clark, E. R.: Arterio-Venous Anastomoses, *Physiol. Rev.* **18**: 229 (April) 1938.

16. Boyd, J. D.: Arterio-Venous Anastomoses, *London Hosp. Gaz. (Clin. Supp.)* **42**: i (July) 1939.

en, is an intraepidermal carcinoma which is primary, as opposed to the "Paget" type of change, which is secondary. In the former, all the characteristics of the primary carcinoma are present and intercellular bridges may be found.

3. *Simple Eczema*.—In simple eczema the microscopic changes in the epidermis are ob-

perplasia, desquamation, edema and hydropic degeneration of epidermal cells.

One finds vesicle formation on the surface, parakeratosis (nucleation of cells in the exfoliative layer), acanthosis (thickening of the epidermis), interstitial edema and chronic inflammatory cell infiltration.



Fig. 7.—Intraepidermal metastatic carcinoma ("Paget's disease") resulting from extension by continuity of adenocarcinoma from underlying breast. Here one can see carcinoma cells arranged in strands filling interstices and lymphatics of the corium. At some points invasion through the basal layer into the epidermis can be seen, and in the layers of the epidermis are seen changes typical of "Paget's disease." These abnormal intraepidermal cells are identical in detail with the carcinoma cells found in the corium and the breast tissue ( $\times 140$ ).

viously not those of malignant processes (fig. 6). The basis of the process is inflammation, with secondary epidermal changes resulting from hy-

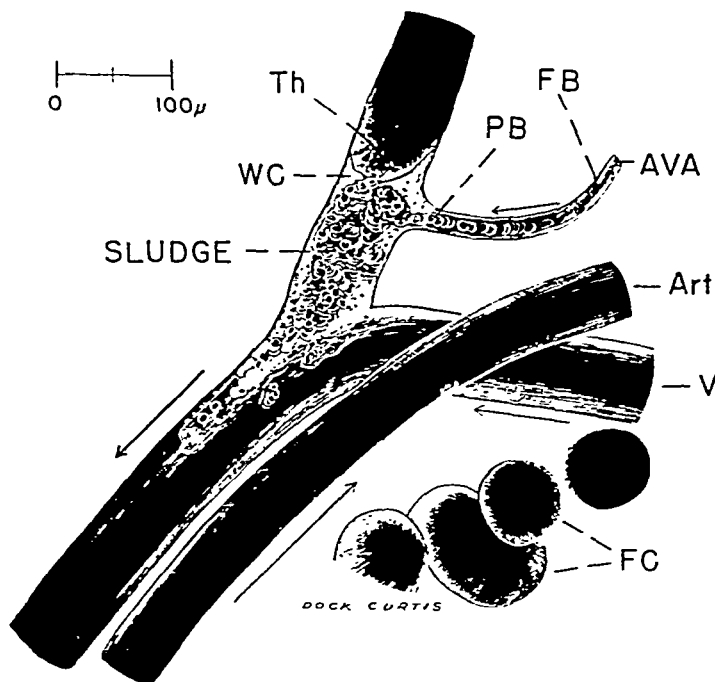
4. *Squamous Carcinoma*.—Of the 1,430 radical mastectomies performed at Barnard Hospital for carcinoma of the breast, in only 3 were there

significantly, probably because all the vessels of the area were by microscopic standards fairly large; arterioles, arteriovenous anastomoses and venules of this size have substantial smooth muscle coats.

6. At the moment the finger was removed from the tissue, few if any white cells were sticking to the walls of injured vessels. However, many of those brought in by the flowing blood adhered to the injured walls. Hence, in a few moments white cells had accumulated one or two and even three layers deep and in irregular masses on injured endothelial surfaces (see the figure and consult E. R. and E. L. Clark<sup>10</sup>).

to determine the precipitation rate (Nygaard<sup>29</sup>), and (c) to record the scene for further study. The scene is somewhat underexposed, satisfactory for research purposes or private showing but not for general distribution.

Copies of this film were later spliced into loops for continuous projection to permit several persons to study the scene together, repeatedly, detail by detail. The outline of the figure is a ciné tracing of the scene, made by projecting the film onto a large sheet of drawing paper while an artist traced the outlines of the stationary structures (Brown and Sheard<sup>30</sup>). Thus these outlines and the scale have about the same accuracy as a good camera lucida drawing. The



Ciné-tracing of a motion picture of blood flowing through crushed monkey omentum. *Art*, artery; *V*, vein; *AVA*, arteriovenous anastomosis; *FC*, fat cells; *Th*, thrombosed venule; *WC*, masses of white cells stuck on inner surface of injured venule; *FB*, fluid blood; *PB*, precipitated blood, and *SLUDGE*, masses of precipitated-agglutinated blood. Note the scale in upper left. Arrows show direction of blood flow. The details of the precipitated-agglutinated blood were added by the artist while studying a looped continuous projection of the scene.

The adhering masses of white cells were continually being bumped by wads of the rapidly moving sludge; from time to time masses of these white cells were forced loose from the vessel lining and carried downstream to the general circulation.

This microscope field was then photographed on Kodachrome motion picture film at 24 frames per second and a Zeiss microscope scale photographed with the same lens combination, in order (a) to measure the dimensions of the structures present, (b) to find out how long it was taking fluid blood to change to thick pasty blood, i. e.,

following additional results were obtained from studies of the film.

7. The blood was fluid at point *FB* and rather solidly precipitated at *PB*. The precipitation end point is not exact, however, nor exactly determinable from the scene. Nor was the precipitation rate constant. Sometimes fairly solid precipitates were formed in blood which had

29. Nygaard, K. K.: Hemorrhagic Diseases—Photo-Electric Study of Blood Coagulability, St. Louis, C. V. Mosby Company, 1941.

30. Brown, G. E., and Sheard, C.: Measurements of the Skin Capillaries in Cases of Polycythemia Vera and the Role of These Capillaries in the Production of Erythrosis, *J. Clin. Investigation* 2: 423 (June) 1926.



Fig. 9.—Secondary epidermal carcinoma ("Paget's disease") resulting from extension along a duct of a primary duct carcinoma of the breast. This section was taken from the margin of the ulcer seen in figure 8 and demonstrates the intraepidermal carcinoma cells identical with the duct carcinoma cells ( $\times 150$ ).



At 6 p. m., ninety minutes later, the following observations were made: 1. The plugs were still present in the two thrombosed venules. 2. The damaged area was still pouring sludged blood into the smaller veins which drained it. A point was found where a venule which came from the damaged area joined one which came from an area of undamaged muscle. Here the experiment and the control were present in one microscope field; it was easy to compare the sludged and the normal blood. There were no free individual cells in the blood passing out of the venule draining the damaged area; all this blood was precipitated and agglutinated into a sludge. 3. No two red cells were sticking together in the blood from the uninjured area; all were free, each turned over by itself unattached to any other—that is, normal blood was flowing through normal vessels in adjacent untraumatized areas of the muscle.

At 6:15 p. m. blood passing through the injured area was still changing to a sludge. At this time, however, there began to be a change. Some of the smallest venules in the injured area had almost normal blood for a few minutes and then sludged blood again. The sludge was being formed intermittently, and the sludge being formed was softer, i. e., the clumps had a fluffy, feathery character rather than a firm, rigid texture. The area was still pouring sludge into the venous system, but there had been a definite decrease in rate of production of sludge, and that produced might better be called a "slush" than a sludge.

It seems reasonable to assume that whatever had been initiating the production of sludge was not reaching or acting in the blood flowing through the injured area as rapidly as during the first ninety minutes after injury.

At 6:30 p. m. the following observations were made. 1. The plugs were still present in the two thrombosed venules. 2. The blood flowing through the injured area was still changing consistency. The sludge formed was less pasty than that formed at first. It was softer, the clumps were more plastic and the rates of flow through these vessels were increasing, approaching the rates through vessels of similar size in the neighboring undamaged areas. The walls of the venules in the injured area were lined with sheets of white cells all rolling along the inner surfaces of the endothelium (E. R. and E. L. Clark<sup>10</sup>). It seemed probable that this injured area would not form sludge much longer. 3. Normal, unagglutinated blood was coming from the uninjured areas.

At 7:30, three hours after the injury, these observations were noted: 1. The two venules originally thrombosed were still plugged up. 2. Patches of slightly agglutinated blood were forming at irregular intervals in blood flowing through the injured area. 3. Normal blood was coming out of the uninjured areas.

At 7:40 the same area was retraumatized by one light wiping stroke of the forceps handle. Immediately the blood flowing through the area became thick and pasty again. This shows that the substances which initiate sludge formation, or their precursors, were not all gone from the injured area.

At 7:55 p. m. the following observations were made: 1. Thrombosed vessels were still thrombosed. 2. Blood flowing through the injured area was still changing to a stiff sludge. 3. Normal blood was coming out of venules of neighboring uninjured muscle.

At 8:15 p. m. there was no change.

At 8:40 p. m. these observations were made: 1. Thrombosed vessels were still thrombosed. 2. All the blood flowing through the injured area was changing to a sludge and passing into the venous system. 3. Normal blood was coming from uninjured areas. The experiment was discontinued.

*Summary of This Experiment with Crushed Mouse Muscle.*—1. A light injury to mouse striated muscle caused precipitation and agglutination of the blood flowing through the injured area. Crush and flow through the crushed muscle were both necessary, and the two together were sufficient to produce a flow of sludged blood into the general circulation.

2. The precipitate was probably being formed in less than half a second.

3. For about one and three-fourths hours after the injury, the rate at which sludged blood was poured into the venous system was as fast as the rate of flow through the crushed area.

4. For the next one and one-fourth hours a progressively decreasing fraction of the blood flowing through this area changed consistency.

5. The clumps formed in the first period were fairly tough and rigid; those formed in the second period were increasingly plastic, flexible and fragile.

6. The visible sludge formed rapidly before the blood left the field being observed. This observation does not mean that all the sludge initiator substances reacted and became inactive within the microscope fields observed. Initiator substances which might be able to cause changes in the blood at some later time and distant place

whether it originated in acinar or duct cells. In only 8 of the 29 cases in this series was there an intraductal carcinoma.

#### EXTRAMAMMARY "PAGET'S DISEASE"

In 1937 H. A. Weiner<sup>14</sup> reviewed the 57 cases which until that time had been reported as instances of "extramammary Paget's disease." He also presented the details of a case of his own. In his patient, he too was able to demonstrate that the intraepidermal cells were, in truth, neoplastic cells extending from a subjacent apocrine gland carcinoma of the vulva. Following a critical study, he concluded that only 15 of the 57 cases so reported entailed sufficient evidence (microscopic examination) to warrant such a diagnosis. In all the acceptable cases the changes occurred in the skin of the areas (axilla and anogenital regions) in which the apocrine sweat glands are present. Of these 15 cases, 9 presented definite evidence of carcinoma elsewhere than in the epidermis, and this in each instance was a glandular carcinoma. In the remaining 6 cases, either no mention was made of cancer or no adequate examination to discover its presence was performed. Others have reported intraepidermal metastatic carcinoma associated with epithelioma, melanoma and rectal carcinoma. Such an observation has led Drake and Whitfield and Civatte (cited by Weiner) to propose that "Paget's disease of the skin" is a nevocarcinoma.<sup>15</sup> Actually, however, a variety of tumors have produced the phenomenon, and it is unreasonable to postulate that all such metastases must be explained on the basis of one particular type.

#### COMMENT

From the evidence obtainable some tenable conclusions may be drawn:

1. Intraepidermal metastatic carcinoma has been repeatedly seen as an accompaniment of

14. Weiner, H. A.: Paget's Disease of the Skin and Its Relation to Carcinoma of the Apocrine Sweat Glands, *Am. J. Cancer* **31**:373-403 (Nov.) 1937.

15. The intraepidermal presence of *thèques* and clear cells in junction type nevi and in melanomas has been repeatedly observed. The clear cell of the junction nevus is easily differentiated from the "Paget cell." Opinion varies here, again, as to the nature of this intraepidermal cell, though from the evidence at hand it appears that the cell originates in the epidermal layer and does not represent an invasion into it. (Becker, S. W.: *Cutaneous Melanoma: A Histologic Study, Especially Directed Toward the Study of Melanoblasts*, *Arch. Dermat. & Syph.* **21**:818-835 [May] 1930. Nicolau, S.: *Sur le phénomène de migration cellulaire intra-épidermique dans le névocarcinome*, *Ann. de dermat. et syph.* **1**:746-762 [July] 1930. Traub, E., and Keil, H.: *The "Common Mole"*, *Arch. Dermat. & Syph.* **41**:214-252 [Feb.] 1940.)

various types of malignant disease variously situated. Some of these metastases have been demonstrated as occurring by variable routes, viz., direct extension, ductal extension or by way of lymphatic channels.

2. The inaccuracy of explaining all such intraepidermal metastatic malignant growths on the basis of a single type of carcinoma is evident, since they may occur from underlying breast carcinoma, from epithelioma, from melanoma, from apocrine gland carcinoma and possibly from others.

3. Much of the difficulty which has arisen in regard to this picture is the result of eponymic labeling of the disease. While due credit should be attributed to Sir James Paget for first calling attention to the relationship between carcinoma of the breast and an eczema-like lesion of the nipple, the term "Paget's disease" has proved unfortunate because it has defeated the very purpose of illustrating this relationship. The placing of all such lesions into a group and labeling them "Paget's disease" has confused not only the clinician who desires to know what he is treating in order that he may treat it adequately but also the pathologist who attempts to theorize on the basis of 1 or several cases as to the nature of what he believes must be an entity, "Paget's disease."

One purpose back of the presentation of this study is to recommend that the terms "Paget's disease of the breast" and "extramammary Paget's disease" be abandoned altogether. The fact that the cells called "Paget cells" are carcinoma cells has been established. No typical and acceptable case of "Paget's disease" which has been adequately studied can be found that is not associated with carcinoma. It is essential to the welfare of such patients, then, that their maladies be recognized as cancer at the earliest possible stage, that is, when the cells are seen in the skin and not when the patient returns with obvious progression following inadequate treatment. When carcinoma cells are discovered in a benign epidermis, they should be called carcinoma cells rather than "Paget cells." In the case of breast lesions, the clinician could and should then treat the malady as a carcinoma primary in the breast, irrespective of palpable mass. In 41 per cent of 29 cases there was no palpable mass when the diagnosis of the skin was made, and yet adenocarcinoma of the breast was demonstrated microscopically. Thus, earlier recognition and earlier treatment of carcinoma in such cases will result.

capillary venules and venules do not leak enough to be detected by microscopic observation.

4. Pentobarbital sodium in anesthetic doses does not cause intravascular agglutination of the circulating blood of *Macacus rhesus* monkeys.

5. Neither pentobarbital sodium nor sodium amytal in anesthetic doses causes intravascular agglutination of the circulating blood of mice.

6. No single factor or combination of factors of the anesthetics used, the withdrawing of the monkey omentum or the brilliant transillumination of tissues whose temperatures are maintained at normal has caused intravascular agglutination of the blood.

7. Laparotomies can be done with sufficient care to prevent general precipitation and agglutination of all the circulating blood.

8. With routine care, normal monkeys have been kept under pentobarbital sodium anesthesia and the circulation in abdominal viscera observed with microscopes without causing general intravascular agglutination of the blood or visible pathologic changes in the walls of small blood vessels for as long as fourteen to eighteen hours.

*II. Methods.*—1. A method is described for maintaining controlled pentobarbital sodium anesthesia of monkeys by intrapleural injections; this is useful for making microscopic observations of abdominal structures.

2. Simple methods are described for studying the vessels and blood of the eyelid, nictitating membrane and bulbar conjunctiva of experimental animals not operated on and of those operated on. The methods have three obvious uses:

(a) To assist in preselecting normal animals for experiments. As agglutinated blood is not normal, as agglutinated blood has already been found as a part of the pathologic change in about forty human diseases and as many of the organisms which affect human beings also affect experimental animals, microscopic observations of the blood and vessel walls are a necessary part of the preselection of normal animals for experiments.

(b) To make continuous observations during the course of experiments on intact animals not operated on to determine the effects of various agents and procedures on the circulating blood and local vessel walls.

(c) To make continuous observations as controls to be certain that during experiments designed with the intention of studying normal animals no agent or procedure is causing mechanical changes in blood and/or pathologic changes in vessel walls.

3. A method is described for studying the blood passing through vessels in or near a minute local lesion. The method should be useful for studying the blood passing through or near lesions caused by many different agents.

*III. Results of Crushing Injuries.*—1. After a crushing injury to monkey omentum, smooth muscle of mouse intestine or striated muscle of a mouse, three zones may be distinguished: (a) a thrombosed zone, (b) a partially crushed or sludging zone and (c) a zone which is injured so little that the blood flowing through it undergoes no detectable change.

(Pentobarbital sodium in monkeys and mice and sodium amytal in mice do not in anesthetic doses prevent the precipitation-agglutination of blood flowing through a crushed area.)

Seen as possible initiating factors in traumatic shock, the observations made in these tissues may be summarized as follows:

2. Crushing plus flow through a vessel in the crushed area yields a stream of sludge into the general circulation.

3. Crushing plus thrombosis of a crushed vessel yields no sludge to the venous system.

4. Flow without crush yields no sludge.

5. Thus, after trauma, (a) local crush plus (b) flow through a vessel in the crushed area are both necessary and, together, sufficient to yield a flow of sludged blood into the general circulation.

6. After crush, precipitates can form around or between the moving blood cells in less than a second, while the blood is moving less than a millimeter.

7. It seems reasonable to suspect that the sludge initiator substances might be related to the substances capable of initiating blood clotting. If this is true, then many tissues and organs of vertebrates should release such substances when they are injured.

8. At no time can sludged blood pass into the venous system faster than the flow through the crushed tissue.

9. For a time after the crush, the rate at which sludge is poured into the venous system can be as fast as the rate of flow through an open vessel in the crushed area.

10. Retraumatization of an area can reinitiate sludge formation in blood flowing through the area.

11. This sludge can be formed in an area from which or into which there is (a) no hemorrhage and (b) but little loss of plasma through injured vessel walls.

# SKELETAL FIXATION OF MANDIBULAR FRACTURES

REPORT OF FIVE CASES, WITH NINE FRACTURES

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AND

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Injuries to the head have been steadily increasing in the past quarter of a century, and fractures of the mandible in particular have increased manifold. The illustration (fig. 1) from Fomon's textbook<sup>1</sup> shows the various sites of fractures and the frequency of occurrence. While this is an accurate and standard chart, the present situation presents a more complex picture. The forces causing head injuries seem to be more intense, with the result that the fractures are frequently multiple and the displacement of the fragments extremely complicating.

Broken jaws have been recorded in medical history since 3,000 B. C., according to Breas-

ment adequate to handle any fracture that was presented. It is still possible for the condyle to be broken so short that pins cannot be inserted. In such a rare instance, an open operation would be mandatory.

Because of the increasing frequency of injuries to the head with the resulting fractures of the mandible and the superior maxilla, we feel that each locality or each hospital should have a group which is interested in such fractures. The ideal team is an oral surgeon, an otolaryngologist and a general surgeon. The oral surgeon contributes his knowledge of the alinement of the teeth and the methods of securing a functioning bite. The otolaryngologist contributes his knowledge of the bones of the face and his ability to handle other fractures of the face as well as other complicating injuries of the head and neck. The general surgeon, with a large practice in fractures, advises as to the alinement of the teeth and the general condition of the patient.

Roger Anderson<sup>3</sup> has been credited with the practical development of the treatment of fractures by external appliance and pin fixation. This is the apparatus that we used. There are other appliances on the market, but we decided to use this because of its simplicity and light weight. It is simple, safe, comfortable and economical.

Gillies<sup>4</sup> listed the advantages of external skeletal fixation: 1. It is available for types of fractures which cannot be treated by other methods. 2. It may be immediately applied to any fracture. There is perfect control of all fragments and anatomic reposition. 3. It permits immediate movement of the temporomandibular joint. 4. It provides for cleanliness of the whole buccal cavity. We found all these advantages, and so far we have found no disadvantages.

We have seen roentgenograms of other patients, in whom the pins were placed too high.

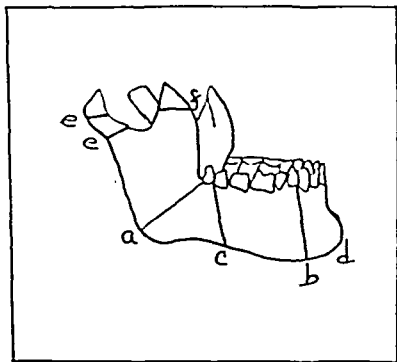


Fig. 1.—Sites of predilection of mandibular fractures, in order of frequency: (a) angle; (b) mental foramen; (c) molar region; (d) symphysis; (e) condyle and (f) coronoid process. (From Fomon.<sup>1</sup>)

ted's<sup>2</sup> translation of the Edwin Smith surgical papyrus. Since this recording of such an injury, there have been numerous methods of treatment. We have tried many of these with varying degrees of success. Until the advent of skeletal fixation, there has not been a universal method of treat-

1. Fomon, S.: *Surgery of Injury and Plastic Repair*, Baltimore, Williams & Wilkins Company, 1939, p. 1203.

2. Breasted, J. H.: *Edwin Smith Surgical Papyrus*, Published in Facsimile and Hieroglyphic Transliteration with Translation and Commentary, Chicago, University of Chicago Press, 1930.

3. Anderson, R.: *Ambulatory Method of Treating Fractures of Shaft of Femur*, *Surg., Gynec. & Obst.* 62:865-873 (May) 1936.

4. Gillies, H. D.: *Replacement and Control of Maxilla Facial Fracture*, *Brit. Dent. J.* 71:351-358 (Dec.) 1941.

mucus and obstruction; the high percentage of oxygen in this inspired closed ether atmosphere allows its almost immediate removal by the blood stream, leaving a collapsed lung behind one or numerous small obstructive masses of mucus.

Cyclopropane was followed by the fewest pulmonary complications as well as other types of complications, in spite of the fact that it is administered to those patients already extremely ill but requiring operation. It causes a negligible amount of bronchial irritation and production of mucus. In a few cases collapse follows administration of cyclopropane, particularly when combined with a large dose of morphine, because of the depression of the respiration from the removal of the carbon dioxide to produce purposely a shallow respiration and a quiet abdomen for surgical intervention.

Aspiration of blood or vomitus during or after operation is an important consideration also, as this may plug the bronchioles. If the airway does not seem to be perfectly clear at the end of operation, this aspiration should be done before the patient is removed to the ward.

The onset of pulmonary collapse occurs suddenly, usually during the first three days, with pain in the chest, dyspnea and a sharp rise in temperature and in pulse and respiration rates. The patient is usually found sitting up in bed, anxious, dyspneic and cyanotic. There is more or less fixation of the affected side, with dullness on percussion, absence of breath sounds, elevation of the diaphragm and shift of the area of cardiac dullness toward the affected side. The unaffected side is hyperresonant, and there are increased breath sounds.<sup>1a</sup> The sputum is scanty at first but quickly becomes abundant and mucopurulent. The white blood cell count may be 15,000 to 20,000. The roentgenogram is characteristic, with elevation of the diaphragm on the affected side, narrowing of the intercostal spaces and deviation of the heart and other mediastinal structures to the affected side, the lung appearing dense and homogenous.

Treatment of such collapse is, of course, primarily prophylactic. As soon as the operative schedule is posted for the following day, the intern on the anesthesia service and I examine each patient and plan the type of anesthetic which will be the best, considering the pathologic condition of the patient, the type of operation proposed and the use of cautery or roentgen ray equipment. A member of the anesthesia department then writes orders for the preoperative medication, giving a small dose of morphine for all patients except those who are young and vigorous. By small dose is meant  $\frac{1}{16}$  grain

(0.0037 Gm.) to  $\frac{1}{8}$  grain (0.007 Gm.) for those above 50 years,  $\frac{1}{8}$  grain to  $\frac{1}{6}$  grain (0.01 Gm.) for those from 50 to about 25 years and  $\frac{1}{6}$  grain for those in good condition, in their twenties and thirties. Occasionally  $\frac{1}{4}$  grain (0.015 Gm.) is given in this group. Scopolamine is given in combination with the morphine preceding spinal anesthesia for further sedation,  $\frac{1}{150}$  grain (0.0004 Gm.) to  $\frac{1}{300}$  grain (0.0002 Gm.) being given with increasing age. Atropine is given preceding an anesthetic administered intravenously, as it has been found that there is more likely to be a fall in blood pressure during the administration of pentothal sodium if it has been preceded by the use of scopolamine. Atropine is also given to young children in preference to scopolamine, which rather seriously depresses them. Administration of the anesthetic is refused until the patient has received atropine or scopolamine for the proper interval previous to operation. Barbiturates are given to all patients preceding use of caudal, epidural or spinal anesthesia to avoid procaine reactions through depression of the central nervous system from stimulation of procaine and its derivatives. Barbiturates are given to those patients to receive nitrous oxide anesthesia to depress the metabolism further, which is necessary when administering this weak gas. They are also given preceding use of cyclopropane to decrease vagal tone and prevent cardiac arrhythmia from the combination of morphine and cyclopropane.<sup>7</sup> Ortol sodium is given to older people, over 50, and pentobarbital sodium in one or two 1.5 grain (0.009 Gm.) doses to younger patients. Seconal when combined with even a small dose of scopolamine has been found to be too depressing to the respirations of old people. Morphine and barbiturates are not given preceding tribromoethanol, as this combination produces severe respiratory depression. At the close of the anesthesia, an attempt is made to have the patient partially awake and to have his pharyngeal reflex back. Nitrous oxide is given during the last few minutes of cyclopropane anesthesia in order to fill the lungs with a substance which is much more slowly absorbed in case a portion of the lung should be cut off behind a mucus plug. Nitrous oxide requires several hours to be dissolved by the blood stream, while cyclopropane and oxygen are removed in a few minutes and in that case would leave a portion of lung collapsed in a short time. I have not seen a case of atelectasis develop after this

7. Robbins, B. H.; Baxter, J. H., and Fitzhugh, O. G.: The Use of Barbiturates in Preventing Cardiac Irregularities Under Cyclopropane or Morphine and Cyclopropane Anesthesia, *Ann. Surg.* **110**:84-93 (July) 1939.

doing regular work on the farm. The pins were removed in the office at the end of eight weeks.

**CASE 3** (figs. 4 and 5).—The patient was a man, aged 8. A roentgenogram showed a transverse fracture of the right mandible at the junction of the horizontal and the ascending ramus which transversed the entire width of the bone, splitting the alveolus of the wisdom tooth. There was a dislocation inward of the proximal fragment. The third molar in the crevice was extracted and four pins inserted, two horizontally and two verti-



Fig. 4.—Perfect alinement of an angle fracture.



Fig. 5.—Placement of pins in an angle fracture.

cally. This patient, as well as the preceding patient, had an excellent resultant bite.

**CASE 4.**—A young woman, aged 28, was injured in an automobile accident. She had a shattering fracture of inferior mandible at the left mental foramen. She also suffered a crushing fracture of the left superior maxilla, with the left alveolar process pushed up to the left orbit. In addition, there were fractures of the right femur and both ankles. The patient was in a state of physical and mental prostration. Her mandible was fixed by skeletal fixation first. Her mental and physical condition cleared at once after the comfortable and permanent fixation of this painful fracture. Three days later the shattered fragments of the left superior

maxilla were molded. The loss of the upper left central incisor, lateral incisor, cuspid, first bicuspid, second bicuspid and first molar greatly weakened the area. The second and third molars were brought into alinement and held in position by a Straith mouth piece. A screw was placed in the left inferior orbital ridge, and this was held out by a bar from a Straith head splint buried in plaster. After these fractures were fixed the other fractures were corrected. The superior maxilla fractures were healed in six weeks; the inferior mandible was held firmly in place for eight weeks. Roentgenograms then showed the fracture firmly healed and so the pins were removed. Prosthetic restoration was satisfactory both from the esthetic and the functional standpoint.

**CASE 5** (figs. 6 and 7).—A girl, aged 18, was a passenger in a pleasure car which was in head-on collision. She suffered no injuries other than four fractures of



Fig. 6.—Four fractures of mandible, bilateral condylar, left angle, and symphysis crushed.



Fig. 7.—Close-up showing how pins were placed to hold all fragments. The plaster cap and supporting rod were used for ten days, as the masseter muscles were so bruised that the patient could not keep her mouth closed, and she complained of her throat becoming dry. In ten days this plaster cap was removed and all motions of the jaw were freely permitted.

at 10:30 a. m., followed by closed ether anesthesia for maintenance. Lysis of extensive adhesions of the omentum into the pelvis was done. The operation lasted an hour and fifty-three minutes, and the patient was returned to the ward in good condition at 12:50 p. m.

sulfate and sulfapyridine. Copious expectoration resulted from cocainization of the throat, with pronounced relief experienced by the patient. A roentgen ray examination at 8 a. m. revealed two-thirds clearing of the left base, with still a slight shift of the mediastinal

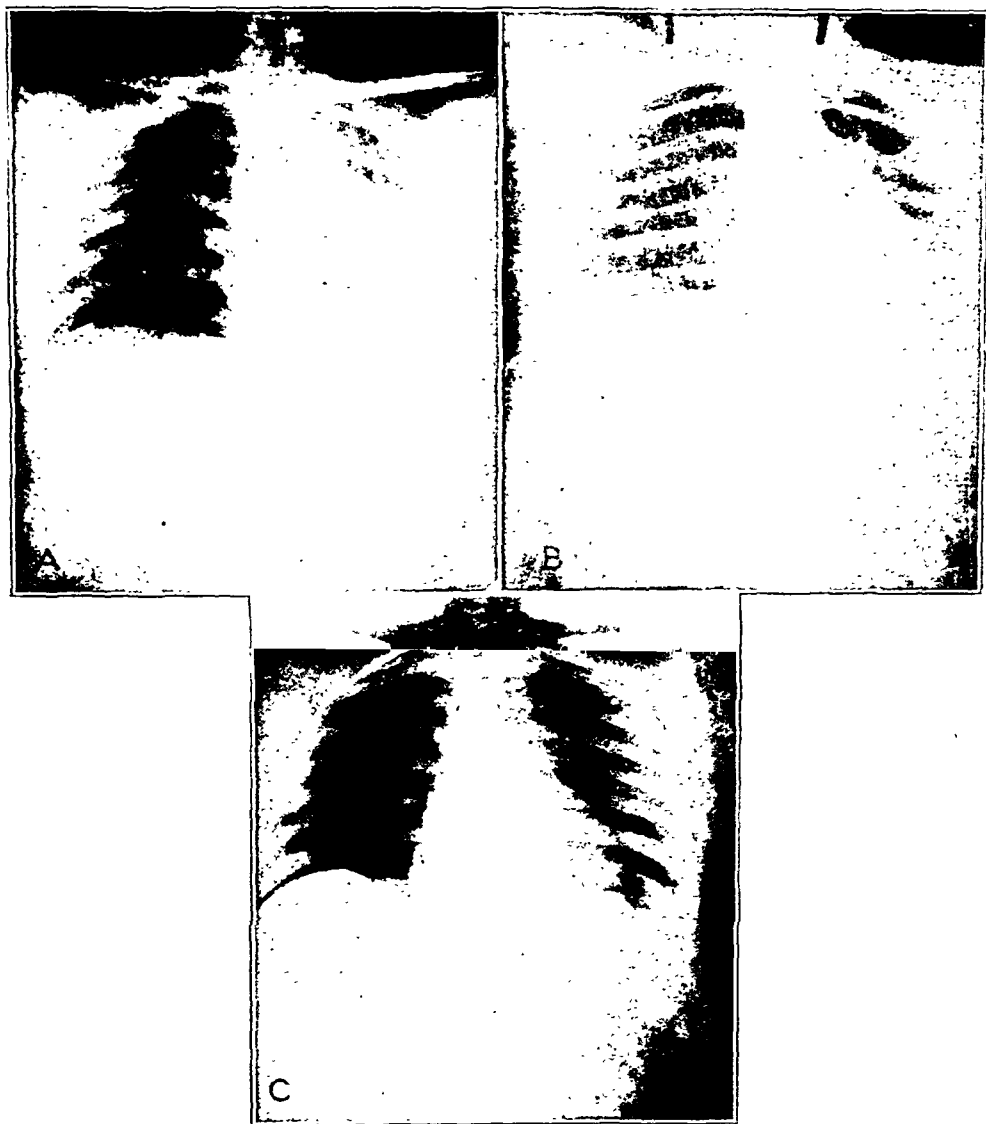


Fig. 2 (case 5).—*A*, showing collapse of the lower lobe of the left lung before treatment. *B*, showing reexpansion of the left base shortly after treatment and two hours after initial collapse. *C*, showing complete reexpansion and clearing of the left lung ten hours after initial collapse, with immediate treatment.

She was talking at 1:50 p. m. At 6 a. m. January 23, she was found cyanotic and complaining of pain in the chest. A roentgenogram revealed collapse of the left lung (fig. 2*A*). Swabbing of the throat with epinephrine and cocaine was started, with inhalations of carbon dioxide and oxygen and use of ammonium

shadow (fig. 2*B*). Roentgen ray examination at 4 p. m. showed complete clearing of the base of the left lung (fig. 2*C*).

This case also illustrates the value of immediate treatment in preventing pneumonia following collapse of the lung.

# PROGRESS IN ORTHOPEDIC SURGERY FOR 1944

A REVIEW PREPARED BY AN EDITORIAL BOARD OF THE AMERICAN  
ACADEMY OF ORTHOPAEDIC SURGEONS

## VI. CONGENITAL DISLOCATION OF THE HIP

PREPARED BY A. BRUCE GILL, M.D., PHILADELPHIA

Turner<sup>170</sup> stresses the importance of early diagnosis and treatment of congenital dislocation of the hip. He feels that complications become worse with delay. The physical signs are listed as: I. Unilateral dislocation: (a) apparent shortening, (b) decrease in range of abduction, (c) piston motion, (d) asymmetry of skin folds about the thighs, (e) palpation of the head of the femur, (f) trochanter affected near the anterior superior spine. II. Bilateral dislocation: (a) wide perineum, (b) apparent lordosis, (c) unusually deep skin folds, (d) trochanters unusually near level of anterior superior spines, (e) palpation of femoral heads. It is noted in the roentgenograms that in congenital dislocation (1) the acetabular roof is sloping more than the normal 170 degrees, (2) the acetabulum is shallow, (3) the epiphysis is smaller, (4) the epiphysis is displaced, (5) Shenton's line is disturbed and (6) the metaphyseal beak is displaced more laterally. The treatment should start as soon as possible. The complications are anteversion of the neck and aseptic necrosis.

Thompson<sup>171</sup> discusses primary acetabular dysplasia as the basic factor in congenital dislocation of the hip. The condition is hereditary and may be transmitted through either side of the family. This dysplasia may be recognized in the early weeks of life by the obliquity and the shallowness of the acetabulum as seen in roentgenograms of the hips. Dislocation may or may not occur, depending on the degree of the imperfection of the acetabulum, but if the dysplasia is not corrected during the period of growth the hip will always be abnormal, even though frank dislocation does not develop.

Natural growth processes will frequently overcome the dysplasia and cause a normal development of the acetabulum and of the head of the

femur if the normal mechanics of the hip are restored and maintained. Early treatments to take advantage of normal growth from the beginning are imperative.

The author reviews the clinical and roentgenographic evidence of "predislocations" of the hip. [ED. NOTE.—I attach more importance to limitation of abduction than to asymmetry of the gluteal folds.] Predislocation should be treated by maintaining the hip in abduction and internal rotation until a roentgenogram shows that the hip has developed normally.

Dislocation should be reduced as soon as the diagnosis is made. Careful bloodless reduction is generally employed. If the dislocation cannot be reduced by manipulation or if reduction is not maintained, open reduction should be performed. Thompson has performed open reduction on a patient at as early an age as 5 months. He believes that the acetabulum develops more rapidly after open reduction than during fixation in a position of incomplete reduction. He advises osteotomy six weeks after open reduction, to correct anteversion of the neck. Fixation in plaster for six months after the open reduction is followed by unrestricted use of the extremity, without further orthopedic treatment. Periodic roentgenographic check-up is advocated thereafter until it is apparent that the hip joint has developed normally.

Lapin<sup>172</sup> discusses predislocation and describes 3 cases of suggestive physical signs of inequality of the two hip sockets, e. g., waddle gait, limp and asymmetry of buttock folds. In all the cases the roentgenologic examination shows normal conditions. A possible explanation offered is that on one side there may be a long capsular ligament or an intracapsular tissue of increased volume.

Michail<sup>173</sup> suggests that poor results in reduction are often due to difficulty of immobilizing

170. Turner, V. C.: Importance of Early Recognition of Congenital Dislocation of the Hip, *M. J. Wisconsin* 43:613-617 (June) 1944.

171. Thompson, F. R.: Early Diagnosis and Early Treatment of Congenital Dislocation (Acetabular Dysplasia) of the Hip, *New York State J. Med.* 44: 1095-1102 (May 15) 1944.

172. Lapin, H.: Pseudocongenital Dislocations of the Hip in Infants: Three Cases, *Arch. Pediat.* 60:649-652 (Dec.) 1943.

(Footnotes continued on next page)



a basis of various experimental evidence, potassium has been suggested in this role.<sup>11</sup> While some recent evidence supports this view,<sup>12</sup> the importance of potassium has not been generally accepted. This is due in part to the fact that previous studies have been confined to changes in the blood or isolated tissues, and consequently quantitative data on the magnitude of the total changes were not available and also because the observed alterations were interpreted in terms of the normal rather than the shocked animal.

The following observations have been made<sup>5</sup> in an attempt to evaluate the significance of the potassium release in traumatic shock:

(a) In a shocked animal the toxicity of administered potassium increases six to nine times above that for a normal animal (chart 3). This is not the result of a general increase in susceptibility to toxic agents, for under similar conditions the toxicity of magnesium and quinidine (used as drug controls) was less than doubled.

(b) The amount of potassium released in shock, as indicated by analyses of the entire injured area and by urinary studies, is toxic for a normal animal when given intravenously or intraperitoneally and for an anuric (nephrectomized) animal when given subcutaneously and is several times the fatal dose for a shocked animal when given by any route (chart 3).

(c) The elevation of serum potassium in the shocked animal cannot be interpreted in terms of the elevation required to kill a normal animal. Rabbits in shock that are killed by injections of potassium chloride show terminal serum potassium levels (13.20 milliequivalent per liter, with a standard error of 0.22) within the same range as those found in shocked rabbits without treatment with potassium chloride that die from shock several hours later (12.08 milliequivalent with a standard error of 0.35). These values are lower than those obtained for normal rabbits that are killed by injections of potassium chloride (16.58 milliequivalent with a standard error of 0.68). These results suggest that the moderate elevations of serum potassium seen in shock may have greater significance than is usually attrib-

uted to them, particularly in relation to the terminal phases of this condition.

Not only is the shocked animal abnormally sensitive to administered potassium. It is possible to produce withdrawal of fluid and sodium from the body by the intraperitoneal injection of dextrose solutions.<sup>13</sup> By the use of this technic, it has been demonstrated that the shocked animal is also highly susceptible to any additional loss of fluid or sodium.<sup>5</sup>

The evidence indicates that these three factors, fluid loss, sodium loss and potassium toxicity, are interdependent. While in shock the magnitude of each change may not in itself be sufficient to produce death, their combined effects augment one another and may have an important influence on mortality in shock.

There are various types and various degrees of shock, in which a variety of other biochemical changes have been shown to exist<sup>14</sup>; like-

13. Schechter, A. J.: Electrolyte and Volume Changes in Fluids Injected into the Peritoneal Cavity, *Yale J. Biol. & Med.* 4:167-185 (Dec.) 1931. Darrow, D. C., and Yan-net, H.: Changes in Distribution of Body Water Accompanying Increase and Decrease in Extracellular Electrolyte, *J. Clin. Investigation* 14:266-275 (March) 1935; Metabolic Studies of Changes in Body Electrolyte and Distribution of Body Water Induced Experimentally by Deficit of Extracellular Electrolyte, *ibid.* 15:419-427 (July) 1936.

14. (a) Russell, J. A.; Long, C. N. H., and Engel, F. L.: Biochemical Studies on Shock: Role of Peripheral Tissues in Metabolism of Protein and Carbohydrate During Hemorrhagic Shock in Rat, *J. Exper. Med.* 79: 1-7 (Jan.) 1944. Engel, F. L.; Harrison, H. C., and Long, C. N. H.: Biochemical Studies on Shock: Role of Liver and Hepatic Circulation in Metabolic Changes During Hemorrhagic Shock in Rat and Cat, *ibid.* 79: 9-22 (Jan.) 1944. Russell, J. A.; Long, C. N. H., and Wilhelmi, A. E.: Biochemical Studies on Shock: Oxygen Consumption of Liver and Kidney Tissue from Rats in Hemorrhagic Shock, *ibid.* 79:23-33 (Jan.) 1944. (b) Shen, S. C., and Ham, T. H.: Studies on Destruction of Red Blood Cells, *New England J. Med.* 229:701-713 (Nov. 4) 1943. (c) Govier, W. M.: Studies on Shock Induced by Hemorrhage: III. The Correlation of Plasma Thiamin Content with Resistance to Shock in Dogs, *J. Pharmacol. & Exper. Therap.* 77:40-49 (Jan.) 1943. (d) Aub, J. C.; Brues, A. M.; Dubos, R.; Kety, S. S.; Nathanson, I. T.; Pope, A., and Zamecnik, P. D.: Bacteria and the Toxic Factor in Shock, *War Med.* 5:71-73 (Feb.) 1944. (e) Prinzmetal, M.; Freed, S. C., and Kruger, H. E.: Pathogenesis and Treatment of Shock Resulting from Crushing of Muscle, *ibid.* 5: 74-79 (Feb.) 1944. (f) Glenn, W. L.; Muus, J., and Drinker, C. K.: Observations on the Physiology and Biochemistry of Quantitative Burns, *J. Clin. Investigation* 22:451-459 (May) 1943. Perlmann, G. E.; Glenn, W. W., and Kaufman, D.: Changes in Electrolytic Pattern in Lymph and Serum in Experimental Burns, *ibid.* 22:627-633 (July) 1943. (g) Ricca, R. A.; Fink, K.; Katzin, L. I., and Warren, S. L.: Effect of Environmental Temperature on Experimental Traumatic Shock in Dogs, *J. Clin. Investigation* 24:127-139

11. Scudder, J.: Shock: Blood Studies as a Guide to Therapy, Philadelphia, J. B. Lippincott Company, 1940.

12. Bywaters, E. G. L., and Popjak, G.: Experimental Crushing Injury, *Surg., Gynec. & Obst.* 75:612-627 (Nov.) 1942. Bywaters, E. G. L.: Ischemic Muscle Necrosis, *J. A. M. A.* 124:1103-1109 (April 15) 1944. Clarke, A. P. W., and Cleghorn, R. A.: Chemical Studies of Tissue Changes in Adrenal Insufficiency and Traumatic Shock, *Endocrinology* 31:597-606 (Dec.) 1942.

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location of the hips. The authors believe that the dislocations are the result of the neural defect produced by the spina bifida. They point out that in severe forms it is accompanied with other anomalies: anencephaly, hydrocephalus, talipes equinus and others. The abnormality most commonly occurs in the lumbosacral region, and the neurologic signs manifest themselves in the lower limbs. Often one group of muscles show fair power, whereas antagonists may show complete paralysis. This was the condition in the 3 cases presented. Urinary incontinence and, less frequently, fecal incontinence are present. Two types of dislocation are distinguished: (1) the endogenous, in which there is a developmental arrest in the acetabular roof, and (2) the dynamic, in which abnormal forces are present, e. g., relaxation of the hip ligaments and imbalance of the muscle. The dislocation usually

occurs in the absence of power of the abductor and external rotator muscles. In the latter cases, maldevelopment of the acetabulum due to disuse follows.

Roberts<sup>177</sup> emphasizes the necessity of constructing the shelf or buttress above the head of the femur in such a manner that the new portion of the acetabulum is molded on top of the head and continues the arc of the circle which is present in the original acetabulum. [Ed. NOTE.—It is often necessary to revise the arc of an oblique acetabulum by reflecting the roof downward.] He describes the method of open reduction and of closing the capsule with sutures so that the capsule overlaps the margin of the newly constructed shelf. He employs a bone strut to fix the iliac bone flap in firm contact with the head.

176. Nathanson, L., and Lewitan, A.: Spina Bifida Associated with Dislocation of the Hip, *Am. J. Roentgenol.* **51**:635-638 (May) 1944.

177. Roberts, F. B.: Plastic Shelf Operation for Dislocations of the Hip, *Ohio State M. J.* **40**:650-656 (July) 1944.

## VII. TUBERCULOSIS OF BONES AND JOINTS

PREPARED BY ALAN DE FOREST SMITH, M.D., AND STAFF OF THE NEW YORK ORTHOPAEDIC DISPENSARY AND HOSPITAL, NEW YORK

During 1944 there were comparatively few articles on the subject of tuberculosis of bones and joints of sufficient interest to include in a review of progress. However, it is encouraging to note an increase in experimental studies toward developing inhibiting or bacteriostatic agents that may be effective against tuberculosis. The effect of a number of sulfonamide compounds, including Diasone and promin, has been studied by a number of investigators, both in the laboratory and on human patients. The results appear to justify the hope that some important result may be expected, although the subject still is in the experimental stage.

In a study by Petter and Prenzlau,<sup>178</sup> Diasone (disodium formaldehyde sulfoxylate diamino-diphenyl sulfone) was therapeutically administered to 78 tuberculous patients for periods ranging from sixty to two hundred and seventy-five days. Seventy-two of the patients had pulmonary lesions, 5 had lesions of bones and joints and 1 had genitourinary lesions. The drug was given orally to all patients and applied locally as well to empyema cavities and abscesses about joints. The dose was usually 0.33 Gm. with meals (1 Gm. per day). Toleration was improved if the drug was started at 0.33 Gm. per

day for three days, increased to 0.66 Gm. for the next three to five days and then raised to the standard dose of 1 Gm. per day. Enteric-coated capsules gave less gastric disturbance. Evidences of toxicity were headache, gastric upset, palpitation, malaise, occasional visual disturbances and "blue skin." Also noted in some patients were an increase in temperature and an increase in cough and expectoration at the onset of treatment. None of these reactions were alarming in severity, none were unbearable and none irreversible. In 3.7 per cent of the cases, the drug was stopped because the patients preferred not to experience the unpleasantness of reactions. Studies of the blood showed an average initial drop from 4,700,000 red cells and 12.5 Gm. of hemoglobin to 2,700,000 red cells and 8.8 Gm. of hemoglobin in the third and fourth weeks and then a gradual rise to about 4,000,000 red cells and 10.3 to 11 Gm. of hemoglobin. Depression of the total leukocyte count did not occur, and neutropenia was not observed. Evidences of damage to the kidneys or liver were not observed clinically or by histologic study in 4 cases coming to autopsy after twelve to seventy-two days of full doses of the drug. With administration of 1 Gm. of Diasone daily, blood levels were maintained between 1.5 and 2 mg. per hundred cubic centimeters. In a small group of cases, the concentration of "free" Diasone in the blood ranged from 1.7 to 2.5 mg., in the cerebrospinal fluid

178. Petter, C. K., and Prenzlau, W. S.: Observation on Clinical Application of Diasone in Human Tuberculosis (Eight Month Study), *Illinois M. J.* **85**: 188-197 (April) 1944.

protein-free ultrafiltrate of serum along with the same serum and also by comparison of serum given by mouth (whereby the proteins as such would not be absorbed) with serum administered intravenously. In these experiments<sup>28</sup> likewise, the therapeutic response could be attributed to the electrolytes contained in the serum (chart 5 A). The results with serum albumin (human) were inferior to those with saline solution or serum and here, again, could be correlated with the amount of electrolyte solution (isotonic solution of sodium chloride) contained in the preparation (chart 4 A).

In contrast to the absence of influence of administration of serum protein was the better therapeutic effect observed in hemorrhage when whole blood or erythrocytes in isotonic solution of sodium chloride were compared with plasma or saline solution alone (chart 5 C).

We have carried out similar studies with whole blood therapy for traumatic and burn shock and were unable to demonstrate any superiority over plasma or isotonic solution of sodium chloride similarly administered. In tourniquet shock, treatment with whole blood, 5 per cent body weight intravenously, brought about a survival of 35 per cent of 32 mice while with plasma 40 per cent survived. In burn shock, similar treatment with whole blood resulted in 42 per cent survivals as compared with 66 per cent with plasma. Thirty to 32 mice were employed in each group, and the control mortalities (untreated mice) were 100 per cent in both experiments.<sup>29</sup>

It is thus observed that under these experimental conditions therapy with whole blood is of value in hemorrhage, but in burn or traumatic shock no superiority over plasma or saline solution could be demonstrated. These observations are of particular interest in view of the recent use of whole blood in the treatment of all forms of shock.

#### OTHER FACTORS

Brief mention will be made of some other factors which we have studied in shock. The harmful effect of an environmental temperature that is too hot or too cold is now well recognized<sup>30</sup>; the exact optimum remains to be

established but available evidence indicates that it lies between 16 and 24 C.<sup>30a</sup>

Administration of 100 per cent oxygen at atmospheric pressure did not affect mortality of burn or tourniquet shock in mice<sup>29</sup>; Frank and Fine have previously reported negative results with oxygen at a pressure of 3 atmospheres for dogs.<sup>31</sup> Morphine in analgesic doses (2 to 6 mg. per kilogram) had no unfavorable influence on burn shock in mice<sup>29</sup>; Blalock has previously reported similar results in dogs.<sup>32</sup> Injection of adrenal cortex extract either prophylactically or subsequent to burns did not affect the acute mortality. Likewise, no therapeutic effect was observed from therapeutic doses of epinephrine in oil or from posterior pituitary extracts.<sup>29</sup> In local therapy of burns, covering two thirds or more of the body surface with tannic acid, liquid petrolatum or cod liver oil was deleterious in that the mortality from shock was increased.<sup>2a</sup>

The immunity which has been observed after repeated trauma has been shown to be a local tissue response rather than a humoral reaction.<sup>33</sup>

#### COMMENT

With simplified procedures it has been possible to study the acute mortality following burns, trauma and hemorrhage in large numbers of small animals. The correction of disturbances of fluids and specific electrolytes has been demonstrated to be of greater importance for survival than the administration of plasma proteins. Our results indicate that for the most favorable response quantities of isotonic solutions of sodium salts equal at least to 10 per cent of body weight are indicated during the first twenty-four hours. In this respect, it is believed that current methods of treating shock are inadequate.

by Environmental Temperature, *Proc. Soc. Exper. Biol. & Med.* **51**:350-351 (Dec.) 1942. Rosenthal.<sup>2a</sup> Ricca, Fink, Katzin and Warren.<sup>14b</sup>

30a. More recent studies of temperature effects<sup>30</sup> have shown that the increased survival time of untreated animals kept at 16 to 22 C. is not a true criterion of optimum temperature. When mice with tourniquet shock are treated with adequate amounts of isotonic solution of sodium chloride or plasma, an entirely different response is obtained; the majority of them will live if kept at 26 to 29 C., while the majority of them will die if kept below 22 C. or above 31 C.

31. Frank, H. A., and Fine, J.: Traumatic Shock: V. A Study of the Effect of Oxygen on Hemorrhagic Shock, *J. Clin. Investigation* **22**:305-313 (March) 1943.

32. Blalock, A.: Effects of Morphine in Experimental Shock Due to Hemorrhage, *Arch. Surg.* **47**:326-328 (Oct.) 1943.

33. Rosenthal, S. M.; Tabor, H., and Lillie, R. D.: The Local Nature of Acquired Resistance to Trauma, *Am. J. Physiol.* **143**:402-406 (March) 1945.

28. Rosenthal.<sup>3</sup> Tabor, Kabat and Rosenthal.<sup>4</sup>

29. Unpublished results.

30. Gatch, W. D., and Wakim, K. G.: Effect of External Temperature on Shock: Experimental Study, *J. A. M. A.* **121**:903-907 (March 30) 1943. Cleghorn, R. A.: The Effect of Different Environmental Temperatures on the Survival of Dogs After Severe Bleeding, *Canad. M. A. J.* **49**:363-367 (Nov.) 1943. Elman, R.; Cox, W. M.; Lischer, C., and Mueller, A. J.: Mortality in Severe Experimental Burns as Affected

Freedlander,<sup>183</sup> in a brief review, states that he has tested some ninety derivatives of benzophenone for their tuberculostatic effect in vitro. Benzophenone is low in toxicity and shows moderately high bacteriostatic action. The following derivatives increased the bacteriostatic action: 4-chloro; 2-chloro; 2,4' dichloro; 2-iodo; 4-methyl; 4-methoxy; 4-ethoxy, and thiobenzophenone. It was not possible to find a definite chemical pattern in the relationship between chemical structure and tuberculostatic action, but an optimal lipid-water solubility ratio was discernible.

Petter<sup>184</sup> published a note to bridge the gap between "news stories" and the appearance of proposed reports in medical literature. Diasone has been used in treatment of 139 patients. It is still an experimental therapeutic agent. Much more must be learned about dosage, toxic reaction, change which takes place in the tuberculous lesions and many other ramifications of such a problem. One cannot be too emphatic at this time in stating that this compound is not ready for even limited distribution until a great amount of investigational work is completed.

Buu-Hoi and Ratsimamanga<sup>185</sup> reported that dihydrochaulmugryl cinnamate in ethyl dihydrochaulmugrate administered to tuberculous guinea pigs resulted during the seventy-eight day period of the experiment in slower development of tuberculosis, a lowered mortality (30 per cent, as compared with 83 per cent in controls) and anatomically more discrete lesions as compared with those of control animals. In tuberculous guinea pigs on a diet low in ascorbic acid, the evolution of tuberculosis is more rapid than that in animals on a diet high in ascorbic acid.

Feldman and Moses<sup>186</sup> reported experiments in which diphteria toxoid failed to exert any significant deterrent effect on tuberculosis experimentally induced in guinea pigs and rabbits.

Callomon and Groskin,<sup>187</sup> using promin, disodium formaldehyde sulfoxalate diaminodiphenylsulfone (compound 2398) and 4( $\alpha$ -pyridil-

N-sulfonamide) phenyl 2-azo-8-amino-1-naphthol 5,7-disulfonic acid (compound 2816), produced evident inhibition of the development of experimental tuberculosis in guinea pigs observed over a period of six weeks. Sulfanilamide, sulfapyridine, sulfathiazole and sulfathiazoline showed no appreciable effect under the same conditions of experimentation. Judged from mortality and histologic change, Promin produced the most beneficial results.

Penicillin, penatin and extracts of Raulin-Thom culture mediums of *Penicillium notatum* and *Penicillium cyclopium* were examined by Smith and Emmart<sup>188</sup> for their bacteriostatic action against tubercle bacillus in vitro, for their inhibiting action of tubercle formation on chorio-allantoic membrane of the chick embryo and for their chemotherapeutic effectiveness against experimental guinea pig tuberculosis. Extracts of the culture medium of *P. notatum* gave good but variable inhibition of growth of tubercle bacilli in glycerin bouillon. All the preparations tested appeared to have some activity in reducing the extent of tubercle formation on the chorio-allantoic membranes but did not decrease the incidence of infection. Penicillin exhibited no effect on experimental tuberculosis in the guinea pig; a slightly favorable effect was obtained with extracts of the culture mediums of *P. notatum*. At best, the chemotherapeutic activity of these preparations was slight compared with some of the sulfones previously investigated by the authors.

Schwartz<sup>189</sup> studied 4 rabbits given subarachnoid-suboccipital injections of tubercle bacilli. Meningitis, meningomyelitis, radiculitis, ganglionitis and tuberculoma developed. Following a review of the literature on experimental spinal tuberculosis, the author stresses the fact that in man the least frequent localization of tuberculoma is in the spinal cord. For the development of tuberculoma, not only the duration of the infection but probably the type and the dose of bacilli play a part. In most of the rabbits, paresis, paralysis and muscular atrophy developed. This is explained by the greater infiltration at the level of the cauda equina, which regulates motor sensibility and trophism of the hindlegs. This localization also favors limitation of the infection.

Hinshaw, Feldman and Pfuertze<sup>190</sup> studied evidence based on the administration of pro-

183. Freedlander, B. L.: Experiments in the Chemotherapy of Tuberculosis, California & West. Med. **61**: 85 (Aug.) 1944.

184. Petter, C. K.: Diasone in Tuberculosis, J. A. M. A. **124**:385 (Feb. 5) 1944.

185. Buu-Hoi and Ratsimamanga, A. R.: Ethyl Dehydrochaulmoograte Combined with Cinnamic Acid Derivatives in Experimental Tuberculosis, Compt. rend. Soc. de biol. **136**:772-774, 1942.

186. Feldman, W. H., and Moses, H. E.: Effect of Diphteria Toxoid on Experimental Tuberculosis, Internat. J. Leprosy **11**:36-42 (Dec.) 1943.

187. Callomon, F. F. T., and Groskin, L.: Therapeutic Effect of Some New Derivatives of di-Amino-di-Phenylsulfone in Experimental Tuberculosis of Guinea Pigs, Tuberculoogy **7**:21-25 (Feb.) 1944.

188. Smith, M. I., and Emmart, E. W.: Action of *Penicillium* Extracts in Experimental Tuberculosis, Pub. Health Rep. **59**:417-423 (March 31) 1944.

189. Schwartz, L.: Experimental Tuberculosis, Día méd. **16**:204-206 (March) 1944.

(Footnotes continued on next page)

The most recent of the absorbable hemostatic materials is gelatin sponge or foam.<sup>11</sup> This is prepared from ordinary commercial gelatin, which is made up in a solution, to which a hardening agent is added. After bubbles of air are introduced, the mixture is allowed to dry in pans. It can then be cut into any desired size or shape. The material which has been used for experimental purposes has been provided in sealed glass jars previously subjected to sterilization with dry heat. The gelatin sponge is a white crisp material which is extremely light in weight. One cubic centimeter weighs 9 mg. The sponge will take up many times its weight of water when it is submerged and the air bubbles expressed.

additional factor in this evaluation, the gelatin sponge was used without thrombin.

A series of 12 dogs was operated on by ordinary aseptic surgical technic with ether anesthesia. After the abdomen had been opened, incisions were made 2 cm. long and 1 cm. deep in the liver, the kidneys and the spleen. The brisk hemorrhage which resulted from these incisions was controlled by packing the moistened gelatin sponge into the incision and holding it in place for about two minutes with ordinary moistened gauze. When the gauze was removed, the gelatin sponge was usually adherent in the incision and the bleeding stopped. Sometimes there was oozing from the ends of the incision, which was arrested by laying another piece of gelatin sponge over the length of the incision and covering the previously applied sponge. Gelatin sponge was also implanted in the

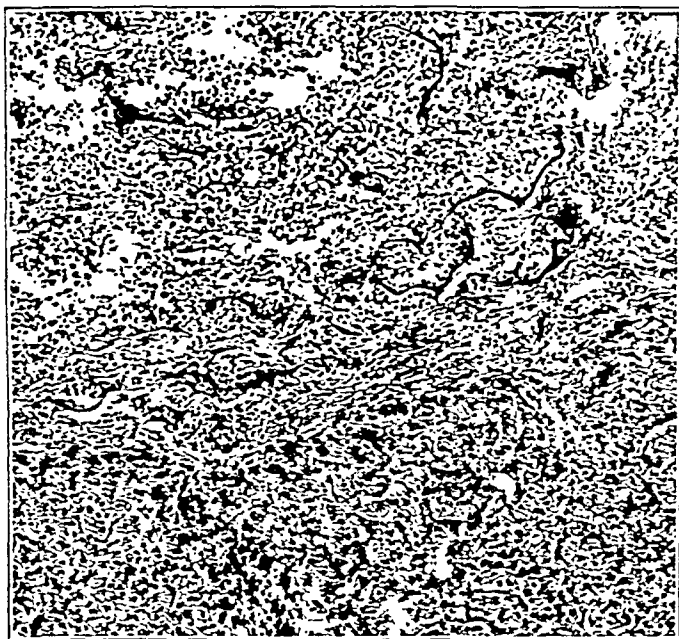


Fig. 2.—Gelatin sponge in liver after seven days. There is a wide zone of polymorphonuclear leukocytic invasion of the sponge at its junction with the liver, the parenchyma of which does not appear to exhibit any inflammatory reaction. The sponge appears to have undergone a considerable degree of absorption, as only fragments remain near the liver.

When moistened, the gelatin sponge shrinks and becomes soft and pliable. It easily adjusts itself to any irregularities in the surface to which it is applied. It does not fragment easily, although it is not especially tough.

#### EXPERIMENTAL STUDY

An experiment was devised primarily to determine the behavior of the gelatin sponge in the tissues of animals and the response of the tissues to the gelatin. To avoid the introduction of an

omentum and in the rectus muscle near the abdominal incision. The animals were killed at periods varying from two to fifty-six days after the implantation. Two of the animals died at two and three days respectively.

At autopsy the sponge could usually be easily identified in the short term implants as a red soggy mass. In the omentum there was an area of induration, in the center of which the sponge could be found if the omentum was cut across at this point. In the abdominal wall one could usually detect a small area of induration along the peritoneal surface (the sponge was put between the posterior sheath and the rectus muscle) which when cut revealed the sponge. After a week or ten days it was often difficult to

11. Correll, J. T., and Wise, E. C.: Certain Properties of a New Physiologically Absorbable Sponge, *Proc. Soc. Exper. Biol. & Med.* 58:233, 1945.

length of the extremity should be made and an epiphysial arrest should be done in the opposite extremity at the appropriate time.

Mordasini<sup>194</sup> discusses the planogram as a valuable addition to the conventional roentgenograms in the diagnosis of tuberculosis in bone. A positive diagnosis can be made earlier. This technic is more useful in the frontal than in the lateral planes in tuberculosis of the spine. Case reports show that the early spinal lesion is not in the anterior part of the vertebra but that it starts in the central or the posterior portion of the body of the vertebra. Narrowing of the intervertebral spaces appears later.

[ED. NOTE.—The laminagraph has been proved to be of value in the detection of areas of tuberculosis of the vertebrae at the New York Orthopaedic Dispensary and Hospital.]

Meng and Wu<sup>195</sup> reviewed 70 cases of tuberculosis of flat bones of the vault, 40 of which had sufficient data for a definite diagnosis. Of the 40 cases, 20 were proved histologically and 5 by guinea pig inoculation or culture; 15 had sufficient clinical signs to justify the diagnosis. Eighty per cent of the patients were under 20 years of age. There were 23 men and 17 women. Trauma was not important or essential but may have been contributory. Eighty-five per cent had associated tuberculous lesions, and 50 per cent had pulmonary tuberculosis. Most lesions were, therefore, secondary hematogenous lesions starting in the diploe, and the tables were involved by extrusion. Two types of lesion are recognized: (a) the circumscribed (perforating) type of Volkmann (38 cases) and (b) the diffuse (infiltrating) type of Koenig (2 cases). There was a single lesion of the skull in 23 cases and multiple lesions in 17 cases. Most frequently involved were the frontal and the parietal bones because they contain a greater amount of cancellous bone. The onset was insidious, with only swelling evident. Pulsation of the mass indicates perforation of both tables. Differential diagnosis includes lipoma, sebaceous cyst, syphilis and

tumor. Results of roentgenologic examination are not typical and show only a round or oval single or a multiple punched-out defect. Aspiration is helpful. Treatment should be complete excision without drainage in the absence of a sinus, and the dura should be let alone. High voltage roentgen rays are sometimes of benefit.

Some of the causes of painful shoulder with radiation of the pain into the arm are discussed by Cohn.<sup>196</sup> No attempt is made to classify all the conditions which cause painful shoulder, but the diseases mentioned, with illustrative cases, are as follows: hypertrophic arthritis of the cervical portion of the spine, carcinoma metastasis to the cervical portion of the spine, herniated cervical intervertebral disk and tuberculosis of the cervical portion of the spine. The author also directs attention to these conditions which may be responsible for pain in the shoulder, i. e., cervical rib, the various neuritides and local lesions of the shoulder region, including arthritis, peri arthritis, bursitis and tears of the supraspinatus tendon. A careful and detailed physical and roentgenographic examination is stressed as a necessary means of securing an accurate diagnosis.

The author observes that referred pain in tuberculosis of bones and joints is a common symptom, and any complaint referable to the shoulder, especially in the absence of definite physical abnormalities, should make one suspicious of a lesion of the cervical portion of the spine. Roentgenographic studies of the cervical portion of the spine should always be made in cases in which pain in the shoulder is the symptom, especially when local signs are absent, because not infrequently advanced changes will be noted on the roentgenogram even when the patient does not complain of symptoms referable to the neck. The author believes that the modus operandi of the referred pain in many cases of tuberculosis of the cervical portion of the spine is due to compression of the nerve roots by tuberculous granulation tissue. The referred pain, as a rule, promptly responds to immobilization of the cervical portion of the spine in a plaster cast.

196. Cohn, B. N. E.: Painful Shoulder Due to Lesions of Cervical Spine, *Am. J. Surg.* 66:269-274 (Nov.) 1944.

194. Mordasini, E.: Beitrag zur Tomographie der Knochen und Gelenke unter besonderer Berücksichtigung der Knochen und Gelenktuberkulose, Schweiz. med. Wchnschr. 74:123 (Feb. 5) 1944.

195. Meng, C. M., and Wu, Y. K.: Tuberculosis of the Flat Bones of the Vault: Forty Cases, Chinese M. J. 61:155-171 (April-June) 1943.

#### VIII. CHRONIC ARTHRITIS

PREPARED BY JOHN G. KUHN, M.D., BOSTON

The appearance of arthritis and rheumatic fever in the armed forces has spurred further investigation and the development of special

services for their treatment. The newer anti-biotic substances have been carefully studied in attempts to prevent or relieve these diseases.

however, there was only a slight invasion of the sponge by polymorphonuclear leukocytes. In addition, there were also lymphocytes and some plasma cells in the peripheral portions.

After a week or more, the predominant cells invading the gelatin sponge were macrophages. There was little tendency for the formation of foreign body giant cells, such as one sees frequently in microscopic sections of suture material such as cotton, silk, linen or chromic surgical

tion became fibrous. In the longer term implants, the fibrous tissue appeared to invade the periphery of the sponge where absorption had occurred as a result of the activity of the macrophages.

In some of the sections there was evidence of the surgical gut suture material which had been used to hold the implant in place. The tissue response to the gut was invariably more pronounced than that observed for the gelatin sponge.



Fig. 4.—Gelatin sponge in liver after twenty-three days. The gelatin sponge is separated from the normal-appearing liver cells by a thin zone of fibrous tissue which merges with and invades the peripheral portion of the sponge. The interstices of the sponge are filled with red blood cells in some areas, and there are a moderate number of macrophages throughout. Polymorphonuclear leukocytes are scarce. There is some thinning out of the walls of the cavernous spaces and some collapsing of the walls, indicative of a moderate degree of absorption.

gut. These macrophages did not form a dense mass of cells, such as one sees at the site of absorption of chromic surgical gut, but rather a more evenly dispersed grouping of cells throughout the interstices of the sponge (figs. 4, 5 and 6).

Fibroblast response was usually observed within a week, producing a definite encapsulation of the sponge. Subsequently this encapsula-

The absorption of the gelatin sponge was apparently most rapid in the presence of polymorphonuclear leukocytes, which appeared to produce a liquefaction of the gelatin sponge. In some such instances, the absorption had progressed almost to completion within twelve days. On the other hand, most of the implants showed evidence of a slower absorption, which appeared to be carried out by macrophages and which

lamage. Thirty-four cases are reported, 6 in detail. The patients had multiple inflammation, with subsidence of all symptoms between attacks. The cause was unknown. Usually the examination of the blood gave normal results, and the erythrocyte sedimentation rate was normal. Attacks provoked only transient slight elevations in the sedimentation rate. Pathologic examination of joints showed an increase in polymorphonuclear leukocytes in the synovial membrane. There might be a fibropurulent exudate. Between attacks, tissues of the joints revealed no significant evidence of inflammation. Treatment for the most part was symptomatic, usually heat and analgesics during attacks. Of 27 patients followed, 15 per cent were well, 44 per cent had improved and 26 per cent were in the same condition. Three patients were worse, and 1 had died. Not a single joint in these patients had been crippled.

[ED. NOTE.—The diagnosis of palindromic rheumatism should be made with great caution. Rheumatoid arthritis often develops slowly. I have recently seen 3 patients who had been studied in a large medical clinic and whose disease had been diagnosed as palindromic rheumatism. These patients later showed pronounced deformities and articular damage.]

Research projects have considered various phases of etiology, pathology and treatment of chronic arthritis. Waite and his associates<sup>205</sup> attempted to determine whether any toxic or infectious substance was excreted in the urine by patients suffering from rheumatoid arthritis. Urine from patients with active rheumatoid arthritis was passed through a filter, and 1 cc. was injected subcutaneously into the abdomens of 3 rats four times a week. Some of the urine was extracted with 70 per cent alcohol after absorption with kaolin. The extract was evaporated under a vacuum. The residuum was taken up in sterile isotonic solution of sodium chloride to make 5 cc. and adjusted to pH 7.4. One cubic centimeter was injected into each of 3 rats. Urine was also extracted with chloroform and evaporated under a vacuum. This was taken up in sesame oil and injected into 3 rats. The animals were killed in four months. No significant lesions were found. Rosenberg and co-workers<sup>206</sup> report the causes

of death of 30 patients suffering from rheumatoid arthritis. They found pulmonary disease the most common, causing death of 11 patients in this series. Cardiac disease was the cause for 9 patients; 7 of these patients had rheumatic heart disease. Renal disease was the cause of death of 3 patients, intestinal disease of 2, and miscellaneous causes of 5—cinchophen hepatitis, accidental death, carcinoma of the prostate, sudden unexplained death and cause unknown. The authors feel that there may be a relationship between unrecognized early rheumatic fever and the large number of deaths from cardiac disease. In only 10 of the patients was death in any way a result of the arthritis. Bayles and Riddell<sup>207</sup> studied the lipemia in three groups of patients with rheumatoid arthritis—10 patients receiving the usual nonspecific therapy, 11 receiving gold salt therapy and 4 whose arthritis was complicated by pregnancy. They found the total lipid, total cholesterol and phosphatide levels of the plasma and the lipid ratio normal in persons with active rheumatoid arthritis. Practically no change was noticed in the patients receiving gold salts. The lipemia of pregnant arthritic patients was similar to that of normal pregnant women. The amelioration observed on arthritis by pregnancy was not dependent on a correction of a lipid deficiency or on a shift in lipid ratios.

To determine the toxicity of gold salts, Freyberg and his associates<sup>208</sup> injected equivalent amounts of gold into rats, using compounds varying widely in their chemical and physical properties. They found that large doses of soluble gold salts (much larger than therapeutic doses) cause severe damage to renal tubules and glomeruli. The severity of the pathologic changes was in direct proportion to the amount of gold injected. No other organs showed important pathologic changes. Suspensions of gold in oil produced lesions in proportion to the solubility of the gold. Colloidal gold caused little renal damage, but reticuloendothelial cells packed with gold were observed in the liver and spleen after its injection. The dosage of gold could not be controlled by study of the plasma concentration of gold. In gold dermatitis, biopsies of the skin showed about the same amount of gold in the skin as was found in the skin of patients receiving gold who had no

205. Waite, H.; Bauer, W., and Bennett, G. A.: Effect of Subcutaneous Injection of Urine and Urinary Extracts from Patients with Rheumatoid Arthritis into Rats, *J. Lab. & Clin. Med.* 29:19-20 (Jan.) 1944.

206. Rosenberg, E. F.; Baggenstoss, A. H., and Hench, P. S.: Causes of Death in Thirty Cases of Rheumatoid Arthritis, *Ann. Int. Med.* 20:903-919 (June) 1944.

207. Bayles, T. B., and Riddell, C. B.: Plasma Lipids in Arthritis Patients Receiving Gold Salt Therapy and During Pregnancy, *Am. J. M. Sc.* 208:343-350 (Sept.) 1944.

208. Freyberg, R. H.; Block, W. D., and Preston, W. S.: Gold Toxicity in Relation to Gold Salt Therapy for Rheumatoid Arthritis, *J. A. M. A.* 124:800 (March) 1944.



this hemostatic substance. Bleeding from tooth sockets can be controlled by gelatin sponge.

The most hopeful use for the gelatin sponge might be as a first aid measure in military combat to pack into bleeding wounds when facilities are not available for the immediate treatment of the wounds. The use of a penicillin solution to moisten the sponge may have sufficient merit that it will be possible to control bleeding as well as infection until the patient is evacuated to a point where facilities permit more adequate care.

There is one point about gelatin sponge which must be considered, the fact that gelatin per se is an extremely good culture medium for bacteria and the introduction into contaminated wounds of a substance which would aid the growth of bacteria would not be without its limitations. It must be considered also that it is desirable to avoid or minimize the use of foreign material in a wound if possible. However, if one has the possibility of a troublesome hematoma to consider, there is justification for utilizing a substance which appears to present fewer hazards to the healing of the wound than a large hematoma.

#### SUMMARY

1. Gelatin sponge or foam was found to be a relatively bland substance which usually undergoes absorption by the phagocytic action of macrophages over a period of about five weeks.
2. The presence of a conspicuous number of polymorphonuclear leukocytes would generally lead to rapid absorption of the sponge within a few days to a week, by a liquefaction process.
3. The magnitude of the tissue reaction to the gelatin sponge during the period of absorption was generally less than that observed for surgical gut.
4. Gelatin sponge has a definite hemostatic action per se when applied to bleeding surfaces with moderate pressure.

#### CONCLUSIONS

Gelatin sponge or foam appears to have properties which make it suitable as an absorbable hemostatic substance and deserves clinical trial in the varied fields of surgery to further evaluate its merits and limitations.

[ED. NOTE.—This is a well considered program for treatment in early rheumatic disease. Treatment cannot be standardized because of the multiplicity of possible causes and complicating factors, but a general outline such as this is helpful. Unfortunately, physicians now get patients late in their disease, when a long period of medical and surgical rehabilitation is required. It will probably require a long period of lay and professional education before this program can be applied effectively.]

In therapeutic attempts against chronic arthritis, the newer antibiotic substances have been used, with indifferent success. Boland and his collaborators<sup>215</sup> report on the use of penicillin in the treatment of active rheumatoid arthritis in an army hospital. In rheumatoid arthritis hemolytic streptococci have always been under suspicion. The blood usually contains antibodies against streptococci, usually agglutinins, in high titer. The skin is usually hypersensitive to extracts of hemolytic streptococci. Ten men were treated for whom the diagnosis of rheumatoid arthritis was definite and in whom the damage was not so severe that irreversible changes in the articular tissues had taken place. These patients were given 1,200,000 to 3,200,000 Oxford units daily. The penicillin was given every three hours for from fourteen to twenty days. There were no untoward reactions, and the changes observed were slight. In 8 patients there were no subjective or objective changes. One patient felt worse. In 1, slight subjective improvement was found. In 1, there was moderate subjective and objective improvement. Results of laboratory tests, including leukocyte count, sedimentation rate and cultures and smears for bacteria in the synovial fluid remained unchanged. The appetite improved in 6 of the 10 patients. The authors felt that penicillin was not of value in the treatment of rheumatoid arthritis.

Powell and Rice<sup>216</sup> used penicillin in treatment of rats which had arthritis caused by a pleuropneumonia-like organism. Treatment with penicillin was ineffective. Gold sodium thiomalate (Myocrysine) was effective in controlling the arthritis but was extremely toxic to the laboratory animals.

215. Boland, E. W.; Headley, N. E., and Hench, P. S.: Treatment of Rheumatoid Arthritis with Penicillin, *J. A. M. A.* **126**:820-823 (Nov. 25) 1944.

216. Powell, H. M., and Rice, R. M.: Ineffective Penicillin Chemotherapy of Arthritic Rats Infected with Pleuropneumonia-Like Organisms, *J. Lab. & Clin. Med.* **29**:372-374 (April) 1944.

Rawls<sup>217</sup> used small doses of gold thioglucose (Solgonal B oleosum), which contained 50 per cent gold, for 100 patients. Five milligrams was given twice a week for three weeks, 10 mg. twice a week for the next three weeks and then 25 mg. once a week. In 42 per cent of the patients toxic symptoms developed. Half of these occurred before 100 mg. of gold had been given. The patients quickly recovered from toxic symptoms in such small doses. The severity and duration of toxic symptoms depended on the dosage. There were no fatalities. In 53 per cent of the patients there was pronounced improvement, with almost complete remission of symptoms. Twenty-one per cent were definitely improved; 12 per cent were slightly improved.

Kennedy<sup>218</sup> used subcutaneous deposits of a sulfonamide compound in powder form in treatment of chronic infectious arthritis. He believes that in chronic rheumatoid arthritis the affected joints and lymph glands become metastatic septic foci. For these patients he uses a drachm (3.9 Gm.) or more of sulfanilamide powder subcutaneously in the affected limb. He states that improvement was observed in 3 chronic cases.

Neostigmine to relieve muscular spasm in rheumatoid arthritis was used by Trommer and Cohen<sup>219</sup> on 19 patients. One cubic centimeter of neostigmine methylsulfate (in a dilution of 1:2000) and 0.6 mg. of atropine sulfate were given every other day. In addition 7.5 to 45 mg. of neostigmine bromide with 0.6 to 1.2 cc. of tincture of belladonna were given daily. Thirteen patients showed decreased muscular spasm, and motions were carried out more readily. The effect following injection comes on in fifteen minutes and may last several days. [ED. NOTE.—The editor has observed the effect of neostigmine in similar dosage on a large number of patients during the past two years. Any beneficial effect observed was slight and transient. No lasting benefit was observed from its use.]

The chronically swollen, painful joint is one of the greatest problems in arthritis. Crowe<sup>220</sup>

217. Rawls, W. B., and others: Analysis of Results Obtained with Small Doses of Gold Salts in Treatment of Rheumatoid Arthritis, *Am. J. M. Sc.* **207**:528-533 (April) 1944.

218. Kennedy, R. T.: Chronic Infective Arthritis and an Experiment with Subcutaneous Deposits of Sulfonamide Powder, *M. J. Australia* **1**:150-152 (Feb. 19) 1944.

219. Trommer, P. R., and Cohen, A.: Neostigmine in the Treatment of Muscle Spasm in Arthritis and Associated Conditions, *J. A. M. A.* **124**:1237-1239 (April 29) 1944.

220. Crowe, H. W.: Treatment of Arthritis with Acid Potassium Phosphate, *Lancet* **1**:563-564 (April 29) 1944.

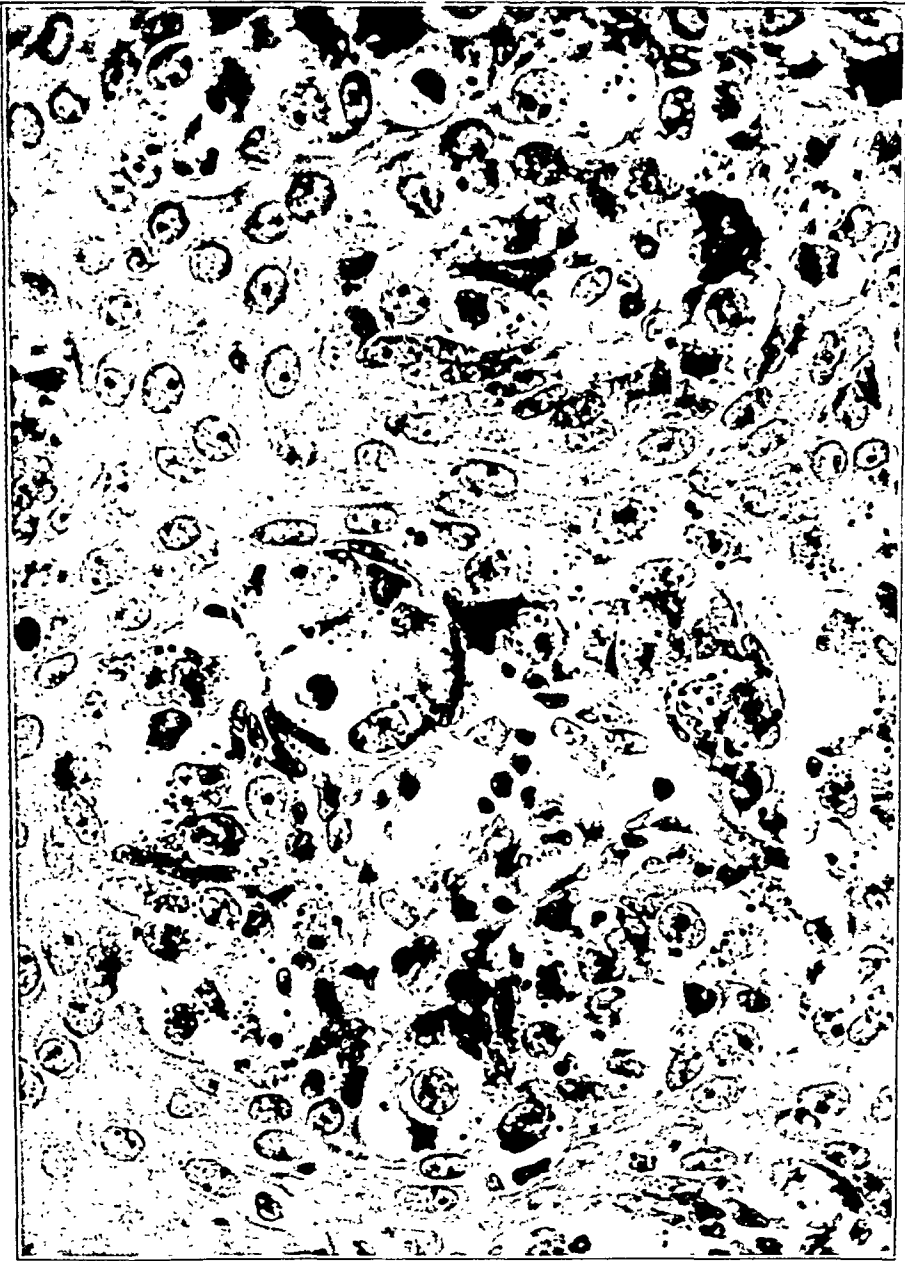


Fig. 2.—A view of the epidermis from a case such as that seen under lower magnification in figure 1 ("Paget's disease"). Here one sees the intraepidermal malignant cells dispersed singly and in bizarre clusters among the epidermal cells. Note that the neoplastic cells ("Paget cells") are generally large and have clear cytoplasm and pyknotic nuclei, and in no instance can be demonstrated intercellular bridges between the abnormal cells and the epidermal cells. The latter characteristic is in favor of the theory that the abnormal cells do not arise in the epidermis. Note also, in this regard, that the contiguous epidermal cells are displaced and compressed by the growth of the neoplastic cells ( $\times 400$ ).

must be followed carefully and carried out by skilled technicians. It is of great help but of itself does not cure.

The role of surgical measures in the treatment of chronic arthritis is discussed by Colonna.<sup>227</sup> The orthopedic surgeon should be responsible for the prevention of deformity and the correction of whatever deformity has developed. In the hip, deformity develops in flexion and adduction, and osteotomy is sometimes required. In the knee the deformity is commonly flexion. An appreciation of the mechanical factors leading to deformity and the mechanical derangements induced by deformity is of prime importance in the rehabilitation of such patients.

A number of papers have considered the diagnosis, complications and treatment of gout.

Sézary and co-workers<sup>228</sup> state that gout is rarely localized to the extremities. They report on a patient in whom deposits of urates provoked inflammatory responses and required removal. [Ed. NOTE.—Faulty diagnosis for such deposits is common until pathologic examination reveals their true character.]

Bauer and Klemperer<sup>229</sup> discuss the medical management of gout. Hyperuricemia may result from decreased destruction, increased formation or decreased elimination of uric acid. In gout it is probably due to limitation of renal excretion of uric acid. Hyperuricemia is not the sole cause of deposition of urates in the tissues. The physiochemical factors which initiate the precipitation of urates are unknown. One cannot use determinations of serum uric acid levels as a measure of the efficiency of treatment, nor can they be used to predict an attack of gout. Colchicum is the drug of choice, but how it acts is unknown, since it does not decrease the hyperuricemia. In the treatment of acute gout, the preliminary use of a saline cathartic is recommended. Colchicine, 0.5 mg., should then be

given every hour until relief of symptoms or toxic symptoms appear—diarrhea, nausea and vomiting. Then one to two doses should be given daily. Fluid, 3,000 to 4,000 cc., and rest in bed should be given. Moist heat over the affected joint is helpful. The prevention of subsequent attacks is difficult; a low purine diet or a fat-free diet is ineffective, and a normal diet is not harmful. As far as can be determined, overindulgence in alcohol does not provoke an attack. Sézary and his colleagues advocate balanced diet, avoidance of foods with high purine content and avoidance of obesity. Colchicine, 0.5 mg. three times a day, with high fluid intake, a high carbohydrate diet and maintenance of an alkaline urine are recommended for long periods. Salicylates, however, are the safest drugs. Acetylsalicylic acid, 5 to 6 Gm. a day, may be used three days a week. This leads to the rapid excretion of uric acid. Attacks cannot be prevented by the continuous use of salicylates. Chronic gouty arthritis is least amenable to treatment. Here pain is due to permanent articular changes. Gout receives no special benefit from spa treatment. The cardiovascular and renal complications are not preventable and must be treated as they appear.

Bartels,<sup>230</sup> in an analysis of the cases of 14 patients with chronic gout, found during an eleven year period an average loss of twenty months from work, an average salary loss of \$3,640 and medical expenses of \$498. In order to prevent such losses, an interval treatment has been planned. This consists of a diet low in purine and fat and high in carbohydrate, with the periodic administration of cinchophen, 7½ grains (0.48 Gm.) three times a day for three days in the week. No alcohol is permitted. Since this diet is low in vitamins A and B, these vitamins are added. At times physical therapy is helpful. Thirty-one cases were studied in detail while the patients were on this regimen. Only seven minor attacks occurred, as compared with eighty-four major attacks during an equal period before treatment.

230. Bartels, E. C.: Successful Treatment of Gout, *J. Tennessee M. A.* 37:5-9 (Jan.) 1944.

227. Colonna, P. C.: Role of Surgery in the Chronic Arthritic Patient, *Clinics* 2:955-965 (Dec.) 1943.

228. Sézary, A.; Boulenger, P., and Malanjeau, P.: *Panaris*, *Presse méd.* 50: 386-387 (June 10) 1942.

229. Bauer, W., and Klemperer, F.: Medical Progress in Gout, *New England J. Med.* 231:681-685 (Nov. 16) 1944.

## IX. INFANTILE PARALYSIS

PREPARED BY C. E. IRWIN, M.D., WARM SPRINGS, GA.

*Etiology.*—Zahorsky's<sup>231</sup> chief purpose is to recall the experiments made by Dr. E. W.

231. Zahorsky, J.: Saunders' Theory on the Etiology of Poliomyelitis, *J. Missouri M. A.* 41:162-164 (Aug.) 1944.

Saunders, who thirty years ago proposed his revolutionary hypothesis on the causation of acute anterior poliomyelitis. This hypothesis, as Dr. Saunders stated, was only a "working hypothesis," to be refuted or corroborated by

TABLE 4.—Summary of Data in 29 Cases of Cancer of the Breast

Case	Age, Yr.	Duration of Cuto- mous Lesion	Pal- pable Mass	Clinical Picture	Pathology	Course
1	45	2 yr.	Yes	Two years ago patient taped both nipples with adhesive tape; right nipple became irritated and has refused to heal; nipple discharged serum and has been seat of constant pruritus; lump present in right breast many years Examination: Right nipple denuded, with raw, moist, bleeding surface; 2 in. (5 cm.) above right nipple is indurated 1 in. (2.5 cm.) nodule; no nodes palpable	Adenocarcinoma of breast, with continuity of carcinoma cells in dermis into epidermis; in addition to intraepidermal extensions, ulceration and chronic inflammatory reaction found	Cutaneous lesion treated with petrolatum dressing for 6 wk., with no improvement; 10/6/22, radical mastectomy performed; 8/22/31, no recurrence demonstrable
2	56	?	No	Patient's mother had carcinoma of the breast; patient scratched by kitten; pruritis and bleeding lesion ensued; no response to treatment with ointment; 40 per cent areola ulcerated and crusted; no nodes palpable	Intraductal carcinoma and intraepidermal malignant cells (Paget); no metastasis to lymph nodes	Biopsy of nipple revealed "Paget's disease"; 11/26/34, radical mastectomy performed; 9/15/41, no recurrence demonstrable
3	51	3 wk.	Yes	Patient aware of lump in left breast for 30 yr.; 3 wk. ago small ulcer developed at dome of left nipple, with no bleeding from lesion of nipple; nipple is verrucous, with crusted, 8 cm. ulcer; palpable mass deep in outer lower quadrant, which is not attached to the skin	Adenocarcinoma of breast and intraepidermal metastasis (Paget's disease of the skin)	10/29/37, simple mastectomy performed, physician believing patient had "cystic disease and keratosis of nipple"; 12/3/37, radical excision of remainder completed; 11/22/41, no recurrence found
4	61	1 yr.	No	Patient noted crusted lesion at tip of left nipple for 1 yr.; "gradually becoming worse" Examination: Reveals such a lesion measuring 4 sq. cm.	(1) Typical "Paget's disease of nipple"; (2) adenocarcinoma of breast, with extensive axillary metastases	(1) 7/29/37, lesion and entire nipple excised; 3/18/38, 3 cm. hard mass in scar and 1 cm. soft nodule in left axilla discovered; (2) 1/1/38, radical mastectomy performed on left side; 11/11/40, patient died from generalized carcinomatosis
5	70	3 yr.	No	For 3 yr. patient had pruritus and burning of right nipple, also ulceration of nipple, with periods of healing Examination: Nipple eroded away by 6 cm. ulcer; no nodes palpable	Intraductal carcinoma; duct lined with malignant cells, extends to skin of nipple and becomes continuous with intraepidermal invasion by malignant "Paget" cells	Simple mastectomy performed (because of patient's age) 7/13/33; 3/17/43, no recurrence
6	63	1 yr.	Yes	One year ago patient observed skin of left nipple "peeling off"; this continued, with no pain or discharge Examination: 2 cm. soft, pink excoriated left nipple; deep in breast tissue in upper outer quadrant is 3 by 1 cm. irregular mass	Biopsy reveals typical intraepidermal malignant cells, with intact basal cell layer; ductal carcinoma in underlying breast ducts	7/28/45, radical mastectomy performed on left side
7	46	6 mo.	Yes	Excised ulcer of left breast present for 6 mo Examination: Superficial erosion of left nipple; subjacent to nipple is irregular hard mass fixed to the skin; hard, movable nodule palpable in left axilla	Adenocarcinoma of breast and at epidermal margin, adenocarcinoma extensions; also in these zones are intraepidermal extensions of same cells, yielding the typical picture of "Paget's disease"	8/11/44, radical mastectomy performed; 12/6/44, no evidence of recurrence
8	46	20 mo.	Yes	Patient discovered induration and pain around right nipple 20 mo. ago; some bloody discharge associated with this Examination: Half of nipple excoriated and granulating; hard fixed subjacent mass palpable in breast	Adenocarcinoma of breast in continuity with epidermal picture of "Paget's disease"; some extensions, in which they appear as "Paget cells"—actually malignant cells	12/3/39, radical mastectomy performed; no recurrence found when patient was last seen, 4/19/40
9	46	5 mo.	Yes	Five months ago patient noted her clothing adhering to left nipple; crust formed, with occasional bloody discharge; small lump noted at same time, which has increased slightly in size Examination: 7 cm. crusted ulcer on left nipple; subjacent to it is 1 cm. mass; 1 cm. hard nodule palpable in left axilla	Adenocarcinoma of breast with lymph node metastases; nipple lesion presents typical picture described as "Paget's disease," with resemblance of "Paget cells" to carcinoma cells of breast	8/9/40, radical mastectomy performed on left side; in 1912 patient died of hypertension
10	46	8 wk.	No	Eight weeks ago patient noted small red spot on left nipple; has had some pruritus	Adenocarcinoma of left breast and changes characteristic of "Paget's disease" in skin of nipple	12/29/40, simple mastectomy performed on left side; 12/29/42, no recurrence; patient not seen since

us organic matter survives more than ten times this amount of residual chlorine.

Arguments against flies playing a role in transmission are as follows: 1. Flies are not invariably associated with the disease, as in winter poliomyelitis. 2. The disease would not attack children preponderantly, as is the case, if it were transmitted primarily by the fly or any other insect. One would expect just such a high incidence in children if adults were immune because of infection—preponderantly abortive or non-paralytic—acquired in childhood or immunity acquired by other, as yet unrecognized, means.

The probability of obtaining virus from flies trapped in epidemic areas would appear to be as good as that of obtaining it from stools and certainly better than that of finding it in nasopharyngeal washings.

Contact infection is admittedly a means of spread, but that it is "the most important means" has not been proved to the authors' satisfaction. Seasonal incidence cannot be explained in this way (epidemics fade out when school opens). The rarity of hospital infection from patient to patient and from patient to hospital personnel would militate against the philosophy of greater segregation as a solution, or even as an aid to a solution, to the problem.

The authors express the belief that it is wise to keep receptive minds to evidence which may eventually show other "modes of spread of infantile paralysis," more in keeping with present knowledge of the natural history of the disease.

Horstmann, Ward and Melnick<sup>235</sup> undertook a study to determine the average duration of excretion of virus in stools of patients following acute infection and to ascertain whether a chronic carrier state similar to that occurring in typhoid exists in poliomyelitis. The stools of 61 patients (46 paralytic and 15 nonparalytic) were collected during the first or second week of the disease and at four to six week intervals thereafter. The materials collected were frozen immediately or within a few hours after collection and stored on solid carbon dioxide until ready to be tested. The inoculum (prepared by Melnick's technic with a few minor changes) was ultracentrifuged at 39,000 revolutions per minute and inoculated into immature rhesus monkeys, by the intracerebral route in fifty-four tests, directly into the lumbar portion of the cord in eighty tests and by a combination of the two routes in twelve. All but 2 monkeys were ultimately killed, and the result of a test

considered positive when microscopic lesions characteristic of poliomyelitis were seen in the spinal cord. It was found that 61 per cent of the patients excreted virus during the first two weeks after onset of the disease, 50 per cent during the third and fourth weeks, 27 per cent during the fifth and sixth weeks and 12.5 per cent during the seventh and eighth weeks. Between the ninth and twenty-fourth weeks, virus was detected in only 1 of 52 specimens tested, 1 patient excreting it in the twelfth week. Not one of the 61 patients followed was demonstrated to become a persistent carrier of poliomyelitis virus.

Maxcy<sup>236</sup> states that present day conceptions of epidemiology of poliomyelitis rest in a large part on the observations made in Norway and Sweden toward the end of the nineteenth century and during the early part of this century, which are available in the classic monograph of Ivan Wickman, published in English translation in 1913. Studies in the United States began with the reports of Dr. Charles S. Caverley on the occurrence of anterior poliomyelitis in the state of Vermont in 1894 and were continued by Flexner and Lewis after the 1907 epidemic in New York and by W. H. Frost after the 1910 outbreak in Minnesota and Nebraska, the 1911 occurrence in Iowa, the outbreak in Cincinnati in 1911 and in Buffalo and Batavia, N. Y., in 1912. The largest epidemic which this country has experienced occurred in and about the city of New York in 1916 and was studied in great detail by three officers of the United States Public Health Service. C. H. Lavinder, A. W. Freeman and W. H. Frost. Since the publication of their report, the large number of contributions from investigators in this country and abroad have served to confirm, amplify and extend the basic observations, although the net advance has been relatively small.

After review of available morbidity and mortality data, with considerations of their limitations in mind, the following brief interpretations regarding broad general characteristics appear to be valid:

1. The disease is worldwide in distribution.
2. From no human community is the disease long absent.
3. Transmission can occur in any month of the year.

235. Horstmann, D. M.; Ward, R., and Melnick, J. L.: Persistence of Virus Excretion in the Stools of Poliomyelitis Patients, *J. A. M. A.* **126**:1061-1062 (Dec. 23) 1944.

236. Maxcy, K. F.: A Review of the Epidemiology of Acute Anterior Poliomyelitis with Reference to the Mode of Transmission, *Journal-Lancet* **61**:216-223 (July) 1944.

ion, is an intraepidermal carcinoma which is primary, as opposed to the "Paget" type of change, which is secondary. In the former, all the characteristics of the primary carcinoma are present and intercellular bridges may be found.

3. *Simple Eczema*.—In simple eczema the microscopic changes in the epidermis are ob-

perplasia, desquamation, edema and hydropic degeneration of epidermal cells.

One finds vesicle formation on the surface, parakeratosis (nucleation of cells in the exfoliative layer), acanthosis (thickening of the epidermis), interstitial edema and chronic inflammatory cell infiltration.



Fig. 7.—Intraepidermal metastatic carcinoma ("Paget's disease") resulting from extension by continuity of adenocarcinoma from underlying breast. Here one can see carcinoma cells arranged in strands filling interstices and lymphatics of the corium. At some points invasion through the basal layer into the epidermis can be seen, and in the layers of the epidermis are seen changes typical of "Paget's disease." These abnormal intraepidermal cells are identical in detail with the carcinoma cells found in the corium and the breast tissue ( $\times 140$ ).

viously not those of malignant processes (fig. 6). The basis of the process is inflammation, with secondary epidermal changes resulting from hy-

4. *Squamous Carcinoma*.—Of the 1,430 radical mastectomies performed at Barnard Hospital for carcinoma of the breast, in only 3 were there

dence suggested that infection occurred at time of birth or shortly thereafter.

Krumbiegel,<sup>238</sup> in discussing the transmission of virus diseases (specifically poliomyelitis) by water, states that pathogens causing communicable diseases known to be spread by water usually enter the body via the gastrointestinal tract and leave in feces or urine or both. Accumulated weight of evidence points toward the gastrointestinal tract as the probable portal of entry, and there are an increasing number of investigators leaning toward the belief that, although poliomyelitis is essentially a disease affecting the central nervous system, it may be a "digestive tract disease" in that the virus may enter the body through one end of the tract and leave by way of the opposite end. Virus is found repeatedly in stools during the second and third weeks of convalescence following paralytic or abortive attacks. Stools are known to have contained virus for as long as one hundred and twenty-three days. The virus is exceedingly stable, surviving a 50 per cent solution of glycerin for eight years, and it withstands low dilutions of phenol and 15 per cent ether. It is not surprising, therefore, that it may be demonstrable in sewage. The activated sludge method of treating sewage is effective in removal or destruction of the virus of poliomyelitis. The virus remains active for as long as one hundred and fourteen days in sterile water at room temperature in the dark. It also withstands freezing. Coagulation and sedimentation seem to produce a slight reduction in the total amount of virus in any suspension, proportional to the amount of virus present. Sand filtration has little if any effect. The addition of activated charcoal to the suspension is partly effective, and the addition of alum floc to the suspension greatly reduces the amount of virus. Chlorination studies are inconclusive, as they were not comparable to methods employed by water purification plants. To date, epidemiologic evidence fails to indicate that water is biologically of any importance as a medium of transmission. It would be necessary to show that the behavior of poliomyelitis in some places or at some times is dependent on contaminated water. This has never been done, and the known epidemiologic behavior of the disease is definitely not compatible with a theory of water-borne spread. Cold is not deleterious to the virus; hence, if water borne, poliomyelitis should occur commonly in winter months. Usually epidemics occur in scattered regions with no common water supply. If the disease

were water-borne, there should be an explosive onset with large numbers of cases, which is not the case. The prevalence of the disease has not been correlated with the degree of sanitary care surrounding different water supplies as determined by either bacteriologic examination or sanitary survey.

Casey and Hidden<sup>239</sup> give a most interesting account of George Colmer III (Kolmer; Sept. 21, 1807-Sept. 27, 1878), a physician who was born in London, England, but who resided at Springfield, Livingston Parish, La., from 1841 until his death, except for a short period when he had an office in New Orleans. His recently discovered "Diary C" covers the period from 1849 to 1878 ("Diaries A and B" have not been found) and records local and national events, clippings from medical and lay journals, pamphlets and advertisements, daily and careful observations on weather, flood stages, flowering of various plants, occurrence of various epidemics, local meetings and local news, such as births, deaths and marriages, observations on garden vegetables, fishing, prize-winning stocks and crops. Another volume, the daily journal of his medical practice from about 1842 to 1878, records brief abstracts of the history, physical examination and treatment of his patients, including two pages of periodic notes on his own physical condition. Dr. Colmer was civic minded and did much for his community, including the building and running of a slave hospital in which the daily board was \$1 and the medical fees in accordance with the malady. His greatest contribution, however, seems to be his observations on the epidemiology of poliomyelitis. Paralysis in children was noted in Philadelphia in 1792 during an epidemic of yellow fever, and 4 cases were noted by Badham in Workshop, England, in 1835. The pathologic changes of poliomyelitis were first described by Heine in 1840, but the first epidemic of the disease to be reported anywhere in the world occurred in 1841 in West Feliciana Parish, La., some 30 miles (48 Km.) from Springfield, La., and was published in *The American Journal of the Medical Sciences* by Dr. Colmer in 1843. His observations that the disease occurred in the form of an epidemic in a small rural area in late summer and fall, that it largely affected children of the teething age (1 to 2 years), that it was associated with paralysis and that most of the youngsters eventually recovered have not been much improved on during the past hundred years. His additional note that teething

238. Krumbiegel, E. R.: Transmission of Virus Diseases by Water, *Bull. Hyg.* 19:513 (July) 1944.

239. Casey, A. E., and Hidden, E. H.: George Colmer and the Epidemiology of Poliomyelitis, *South. M. J.* 37:471-477 (Sept.) 1944.



whether it originated in acinar or duct cells. In only 8 of the 29 cases in this series was there an intraductal carcinoma.

#### EXTRAMAMMARY "PAGET'S DISEASE"

In 1937 H. A. Weiner<sup>14</sup> reviewed the 57 cases which until that time had been reported as instances of "extramammary Paget's disease." He also presented the details of a case of his own. In his patient, he too was able to demonstrate that the intraepidermal cells were, in truth, neoplastic cells extending from a subjacent apocrine gland carcinoma of the vulva. Following a critical study, he concluded that only 15 of the 57 cases so reported entailed sufficient evidence (microscopic examination) to warrant such a diagnosis. In all the acceptable cases the changes occurred in the skin of the areas (axilla and anogenital regions) in which the apocrine sweat glands are present. Of these 15 cases, 9 presented definite evidence of carcinoma elsewhere than in the epidermis, and this in each instance was a glandular carcinoma. In the remaining 6 cases, either no mention was made of cancer or no adequate examination to discover its presence was performed. Others have reported intraepidermal metastatic carcinoma associated with epithelioma, melanoma and rectal carcinoma. Such an observation has led Drake and Whitfield and Civatte (cited by Weiner) to propose that "Paget's disease of the skin" is a nevocarcinoma.<sup>15</sup> Actually, however, a variety of tumors have produced the phenomenon, and it is unreasonable to postulate that all such metastases must be explained on the basis of one particular type.

#### COMMENT

From the evidence obtainable some tenable conclusions may be drawn:

1. Intraepidermal metastatic carcinoma has been repeatedly seen as an accompaniment of

14. Weiner, H. A.: Paget's Disease of the Skin and Its Relation to Carcinoma of the Apocrine Sweat Glands, *Am. J. Cancer* **31**:373-403 (Nov.) 1937.

15. The intraepidermal presence of *thèques* and clear cells in junction type nevi and in melanomas has been repeatedly observed. The clear cell of the junction nevus is easily differentiated from the "Paget cell." Opinion varies here, again, as to the nature of this intraepidermal cell, though from the evidence at hand it appears that the cell originates in the epidermal layer and does not represent an invasion into it. (Becker, S. W.: Cutaneous Melanoma: A Histologic Study, Especially Directed Toward the Study of Melanoblasts, *Arch. Dermat. & Syph.* **21**:818-835 [May] 1930. Nicolau, S.: Sur le phénomène de migration cellulaire intra-épidermique dans le névocarcinome, *Ann. de dermat. et syph.* **1**:746-762 [July] 1930. Traub, E., and Keil, H.: The "Common Mole," *Arch. Dermat. & Syph.* **41**:214-252 [Feb.] 1940.)

various types of malignant disease variously situated. Some of these metastases have been demonstrated as occurring by variable routes, viz., direct extension, ductal extension or by way of lymphatic channels.

2. The inaccuracy of explaining all such intraepidermal metastatic malignant growths on the basis of a single type of carcinoma is evident, since they may occur from underlying breast carcinoma, from epithelioma, from melanoma, from apocrine gland carcinoma and possibly from others.

3. Much of the difficulty which has arisen in regard to this picture is the result of eponymic labeling of the disease. While due credit should be attributed to Sir James Paget for first calling attention to the relationship between carcinoma of the breast and an eczema-like lesion of the nipple, the term "Paget's disease" has proved unfortunate because it has defeated the very purpose of illustrating this relationship. The placing of all such lesions into a group and labeling them "Paget's disease" has confused not only the clinician who desires to know what he is treating in order that he may treat it adequately but also the pathologist who attempts to theorize on the basis of 1 or several cases as to the nature of what he believes must be an entity, "Paget's disease."

One purpose back of the presentation of this study is to recommend that the terms "Paget's disease of the breast" and "extramammary Paget's disease" be abandoned altogether. The fact that the cells called "Paget cells" are carcinoma cells has been established. No typical and acceptable case of "Paget's disease" which has been adequately studied can be found that is not associated with carcinoma. It is essential to the welfare of such patients, then, that their maladies be recognized as cancer at the earliest possible stage, that is, when the cells are seen in the skin and not when the patient returns with obvious progression following inadequate treatment. When carcinoma cells are discovered in a benign epidermis, they should be called carcinoma cells rather than "Paget cells." In the case of breast lesions, the clinician could and should then treat the malady as a carcinoma primary in the breast, irrespective of palpable mass. In 41 per cent of 29 cases there was no palpable mass when the diagnosis of the skin was made, and yet adenocarcinoma of the breast was demonstrated microscopically. Thus, earlier recognition and earlier treatment of carcinoma in such cases will result.

o simulate other disease. The critical findings of differential diagnostic value depend on signs of cord, brain and nerve irritation and must be supported by physical findings. These are sometimes so extremely variable and changeable that they may be detected only by careful, deliberate and repeated examinations. The most important sign is nuchal rigidity, which is accompanied with or followed by spinal tenderness. Kernig's sign may appear early or not. Deep reflexes are present but variable (hyperactive to sluggish). The muscle groups or muscles presenting tremors are likely to be involved. Rigidity of muscles, deep tenderness, discrete areas of perspiration, irritation of rectal or vesical centers in the lumbar part of the cord, with resulting constipation or urine retention, all may be demonstrated. Bulbar involvement may have a rapid onset, with difficulty in swallowing, impairment of phonation, salivation and excessive mucous secretion, disorientation, delirium and coma.

Puncture of the lumbar part of the cord is of therapeutic value in reducing intracranial pressure. The spinal fluid is normal throughout the first febrile and asymptomatic stages of the disease. At the onset of the paralytic phase, the spinal fluid is clear, there is increased pressure, the cells may vary from 10 to 200, the total protein is increased and the fluid is sterile on bacteriologic examination and does not contain the virus. Hence, examination of the spinal fluid is important if the results are positive but not necessarily contradictory when values are normal. The blood count and sedimentation rate are not contributory to diagnosis. Differential diagnosis is important in acute poliomyelitis to rule out purulent meningitis, encephalitis, St. Louis encephalitis and occasionally acute arthritis. The cardinal points of early diagnosis are: (1) awareness of poliomyelitis, (2) history of febrile attack a few days previously, (3) headache and fever, (4) nuchal rigidity and spinal tenderness, (5) spasm, tremor or weakness in a muscle or muscle groups, (6) hyperesthesia or pain, (7) reflex changes and (8) cerebrospinal fluid changes if positive. The author states that (9) the serious grade of the disease is indicated by progressive course and that (10) it is impossible to diagnose subclinical cases in the acute stage.

*Prevention.*—Lumsden,<sup>242</sup> in writing on the epidemiology of poliomyelitis and measures for its prevention, states that the possibility of sev-

eral specific viruses of poliomyelitis is given weight by the fact that strains of the virus obtained in different outbreaks present pronounced differences biologically, serologically, immunologically and otherwise. There are many possible modes of transmission, but none are conclusive. Preventive measures suggested are: (1) cleanliness and maintenance of cleanliness (hygiene and sanitation); (2) systematic, intense and continuous fights on rats, mice, flies, mosquitoes, roaches, fleas, bedbugs, ants, insects and vermin; (3) strict sanitation regarding disposal of garbage, manure and excreta of poultry and birds; (4) screening of living and sleeping quarters; (5) purified water supplies and sanitary sewage systems with final disposal; (6) rigid sanitary and hygienic supervision of public eating and drinking places; (7) educational campaign to discourage potential droplet infection (coughing, sneezing, spitting, blowing and wiping); (8) reasonable discouraging of public assemblages by children under 6 years, and (9) restraining of young children from undue physical stress. Closing of schools, churches and theaters, as is often demanded by misled public opinion, is unjustified; placarding of the affected homes is advisable; proper isolation of patients is advisable to guard against superimposed infections. There should be rigid disinfection of discharges from nose and mouth and feces. Quarantine is not justified except for food handlers and persons in close contact with large numbers of children.

*Pathology.*—Dublin, Bede and Brown<sup>243</sup> report their findings on studies of muscles taken for biopsy from 3 patients with poliomyelitis and stained by the Ranvier method. They observed a degeneration of nerve fibers, motor end plates and muscle fibers in a degree commensurate with the degree of paralysis: an irregularity of distribution in keeping with an irregularity of distribution of injury to nerve cells of the gray matter of the spinal cord; a degeneration of nerve fibers, consisting largely in failure of axons to stain together with preservation of cellular elements of capsules of motor endings and of sheaths of Schwann; atrophy of muscle fibers appearing as pyknosis, beginning with loss of cross striations and increase of longitudinal markings; degeneration of muscle and nerve ranking probably secondary to injury to nerve cells of the spinal cord, and no definite evidence of activity of degeneration or regeneration.

242. Lumsden, L. L.: Poliomyelitis: Its Epidemiology and Measures for Its Prevention. *Texas Rep. Biol. & Med.* 1:233-241, 1943.

243. Dublin, W. B.; Bede, B. A., and Brown, B. A.: Pathologic Findings in Nerve and Muscle in Poliomyelitis. *Am. J. Clin. Path.* 14:266-272 (May) 1944.

doing regular work on the farm. The pins were removed in the office at the end of eight weeks.

CASE 3 (figs. 4 and 5).—The patient was a man, aged 8. A roentgenogram showed a transverse fracture of the right mandible at the junction of the horizontal and the ascending ramus which transversed the entire width of the bone, splitting the alveolus of the wisdom tooth. There was a dislocation inward of the proximal fragment. The third molar in the crevice was extracted and four pins inserted, two horizontally and two verti-

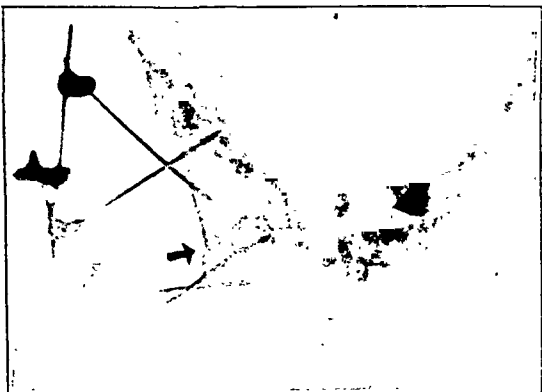


Fig. 4.—Perfect alinement of an angle fracture.



Fig. 5.—Placement of pins in an angle fracture.

cally. This patient, as well as the preceding patient, had an excellent resultant bite.

CASE 4.—A young woman, aged 28, was injured in an automobile accident. She had a shattering fracture of inferior mandible at the left mental foramen. She also suffered a crushing fracture of the left superior maxilla, with the left alveolar process pushed up to the left orbit. In addition, there were fractures of the right femur and both ankles. The patient was in a state of physical and mental prostration. Her mandible was fixed by skeletal fixation first. Her mental and physical condition cleared at once after the comfortable and permanent fixation of this painful fracture. Three days later the shattered fragments of the left superior

maxilla were molded. The loss of the upper left central incisor, lateral incisor, cuspid, first bicuspid, second bicuspid and first molar greatly weakened the area. The second and third molars were brought into alinement and held in position by a Straith mouth piece. A screw was placed in the left inferior orbital ridge, and this was held out by a bar from a Straith head splint buried in plaster. After these fractures were fixed the other fractures were corrected. The superior maxilla fractures were healed in six weeks; the inferior mandible was held firmly in place for eight weeks. Roentgenograms then showed the fracture firmly healed and so the pins were removed. Prosthetic restoration was satisfactory both from the esthetic and the functional standpoint.

CASE 5 (figs. 6 and 7).—A girl, aged 18, was a passenger in a pleasure car which was in head-on collision. She suffered no injuries other than four fractures of

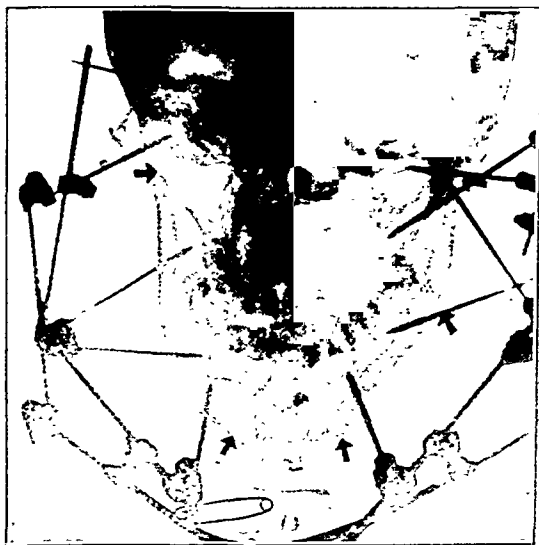


Fig. 6.—Four fractures of mandible, bilateral condylar, left angle, and symphysis crushed.



Fig. 7.—Close-up showing how pins were placed to hold all fragments. The plaster cap and supporting rod were used for ten days, as the masseter muscles were so bruised that the patient could not keep her mouth closed, and she complained of her throat becoming dry. In ten days this plaster cap was removed and all motions of the jaw were freely permitted.

2 cases of Bell's palsy followed by a case of paralytic poliomyelitis in the same family is highly improbable, it is suggested that the virus of poliomyelitis may have involved the nucleus of the seventh cranial nerve, just as it is known to attack the anterior horn cells of the spinal cord. Four years after the onset of the disease, both sisters exhibited a slight residual paralysis of the face and the brother a persisting flaccid paralysis of the right leg.

That additional information might be gained on the relation of tonsillectomy to poliomyelitis the records of the Manhattan Eye, Ear and Throat Hospital were consulted, and many thousands of patients for whom tonsillectomy had been performed were communicated with by mail. Page<sup>247</sup> reports on these data along with the records secured from the New York Department of Health, which showed a conspicuous increase in the number of poliomyelitis cases every other year as follows: 243 cases in 1937, 43 cases in 1938, 184 cases in 1939, 67 cases in 1940 and 404 cases in 1941. Of the 27,849 questionnaires sent out from the hospital, 8,915 were answered, and 1 instance of poliomyelitis was reported. Seven patients reported illnesses following tonsillectomy and adenoidectomy, and all of these mentioned some spinal involvement; 6 reported spinal meningitis (three months to four years after operation) and 1 a "spinal condition which causes nervousness" in a child aged 6.

Howe, Wenner, Bodian and Maxcy<sup>248</sup> report on the different technic used for demonstrating virus in the human nose and throat, which was employed at the New Haven Hospital in the summer of 1943. The attempt to vary the method employed in the past was made, since the attempts of the earlier years have been virtually abandoned in the face of readily isolated intestinal virus. Cotton swabs rubbed against the posterior wall of the oropharynx and the peritonsillar area were dropped into a fluid-tight container with 1 cc. of sterile water, stored on solid carbon dioxide and then eluted in phosphate buffer at  $p_H$  8, the fluid being pressed out of the cotton in a syringe. The eluate was then brought to  $p_H$  6 and treated with 20 per cent ether in the refrigerator until sterile (usually thirty-six hours), at which time the ether was removed. The entire inoculum obtained (in no case more than 1.1 cc.) was given to

rhesus monkeys of 8 to 10 pounds (3.6 to 4.5 Kg.) under ether anesthesia through a trephine hole made over the sagittal suture just posterior to the coronal sutures. An average of two swabs were obtained from 10 patients (paralytic or nonparalytic) during the first week of the acute illness. Fourteen specimens were used from the twenty collected, and seven (50 per cent) produced typical poliomyelitis in the test rhesus monkeys. Microscopic sections showed characteristic lesions in each case.

*Surgical Treatment.*—Debrunner<sup>249</sup> discusses a case of poliomyelitis in which not only organs and tissues were adapted to changed function but function itself was adjusted to changes in structure. A 4 year old girl with residual paralysis in the left leg, slight Trendelenburg position, pes cavus and pronounced paralysis in the heads of both biceps muscles and in the gluteal muscles was observed. In the foot there was a total paralysis of the anterior tibial and pronounced weakening of both other supinators. Her gait was impaired by faulty position of the foot, bearing weight only on the inner margin. She had received no planned treatment. To raise the foot, a small support was made from a plaster cast, which permitted walking in good position. After a year the support had to be altered slightly. A year later, when the mother came for repair of the support, it was noted that the impression of the sole had been changed to that of a normal foot. It is of special interest that a muscle of only secondary importance for the posture mechanism of the foot was brought into use for gait automatism. It is suggested that deformity might be prevented by training motor function.

Wiesenfeld<sup>250</sup> reviews the results of 17 cases of posterior bone block operations: 52.9 per cent were done by Briggs's modification of the Campbell bone block and 35.2 per cent were done by Gill's procedure. All the patients had had previous foot stabilizations. Of the series, 11.9 per cent had a combination foot stabilization, tendo achillis lengthening and posterior bone block. The results were considered excellent in 88.2 per cent of the patients operated on. There were two failures: in the first patient a painful arthritis of the ankle joint developed,

247. Page, J. R.: Tonsillectomy and Poliomyelitis. *Arch. Otolaryng.* 39:323-324 (April) 1944.

248. Howe, H. A.; Wenner, H. A.; Bodian, D., and Maxcy, K. F.: Poliomyelitis Virus in the Human Oropharynx. *Proc. Soc. Exper. Biol. & Med.* 56:171-172 (June) 1944.

249. Debrunner, H.: A Case of Physiologic Functional Adaptation of Plantar Muscles in Residual Paralysis. *Schweiz. med. Wchnschr.* 73:965 (Aug. 7) 1943.

250. Wiesenfeld, P. C.: Report of Seventeen Cases of Posterior Bone Block for Drop-Foot Seen and Treated at the New Jersey Orthopaedic Hospital, Orange, N. J., from 1933 to 1943. *J. M. Soc. New Jersey* 41:344-346 (Sept.) 1944.

location of the hips. The authors believe that the dislocations are the result of the neural defect produced by the spina bifida. They point out that in severe forms it is accompanied with other anomalies: anencephaly, hydrocephalus, talipes equinus and others. The abnormality most commonly occurs in the lumbosacral region, and the neurologic signs manifest themselves in the lower limbs. Often one group of muscles show fair power, whereas antagonists may show complete paralysis. This was the condition in the 3 cases presented. Urinary incontinence and, less frequently, fecal incontinence are present. Two types of dislocation are distinguished: (1) the endogenous, in which there is a developmental arrest in the acetabular roof, and (2) the dynamic, in which abnormal forces are present, e. g., relaxation of the hip ligaments and imbalance of the muscle. The dislocation usually

occurs in the absence of power of the abductor and external rotator muscles. In the latter cases, maldevelopment of the acetabulum due to disuse follows.

Roberts<sup>177</sup> emphasizes the necessity of constructing the shelf or buttress above the head of the femur in such a manner that the new portion of the acetabulum is molded on top of the head and continues the arc of the circle which is present in the original acetabulum. [Ed. NOTE.—It is often necessary to revise the arc of an oblique acetabulum by reflecting the roof downward.] He describes the method of open reduction and of closing the capsule with sutures so that the capsule overlaps the margin of the newly constructed shelf. He employs a bone strut to fix the iliac bone flap in firm contact with the head.

176. Nathanson, L., and Lewitan, A.: Spina Bifida Associated with Dislocation of the Hip, *Am. J. Roentgenol.* 51:635-638 (May) 1944.

177. Roberts, F. B.: Plastic Shelf Operation for Dislocations of the Hip, *Ohio State M. J.* 40:650-656 (July) 1944.

## VII. TUBERCULOSIS OF BONES AND JOINTS

PREPARED BY ALAN DE FOREST SMITH, M.D., AND STAFF OF THE NEW YORK ORTHOPAEDIC DISPENSARY AND HOSPITAL, NEW YORK

During 1944 there were comparatively few articles on the subject of tuberculosis of bones and joints of sufficient interest to include in a review of progress. However, it is encouraging to note an increase in experimental studies toward developing inhibiting or bacteriostatic agents that may be effective against tuberculosis. The effect of a number of sulfonamide compounds, including Diasone and promin, has been studied by a number of investigators, both in the laboratory and on human patients. The results appear to justify the hope that some important result may be expected, although the subject still is in the experimental stage.

In a study by Petter and Prenzlau,<sup>178</sup> Diasone (disodium formaldehyde sulfoxylate diamino-diphenyl sulfone) was therapeutically administered to 78 tuberculous patients for periods ranging from sixty to two hundred and seventy-five days. Seventy-two of the patients had pulmonary lesions, 5 had lesions of bones and joints and 1 had genitourinary lesions. The drug was given orally to all patients and applied locally as well to empyema cavities and abscesses about joints. The dose was usually 0.33 Gm. with meals (1 Gm. per day). Toleration was improved if the drug was started at 0.33 Gm. per

day for three days, increased to 0.66 Gm. for the next three to five days and then raised to the standard dose of 1 Gm. per day. Enteric-coated capsules gave less gastric disturbance. Evidences of toxicity were headache, gastric upset, palpitation, malaise, occasional visual disturbances and "blue skin." Also noted in some patients were an increase in temperature and an increase in cough and expectoration at the onset of treatment. None of these reactions were alarming in severity, none were unbearable and none irreversible. In 3.7 per cent of the cases, the drug was stopped because the patients preferred not to experience the unpleasantness of reactions. Studies of the blood showed an average initial drop from 4,700,000 red cells and 12.5 Gm. of hemoglobin to 2,700,000 red cells and 8.8 Gm. of hemoglobin in the third and fourth weeks and then a gradual rise to about 4,000,000 red cells and 10.3 to 11 Gm. of hemoglobin. Depression of the total leukocyte count did not occur, and neutropenia was not observed. Evidences of damage to the kidneys or liver were not observed clinically or by histologic study in 4 cases coming to autopsy after twelve to seventy-two days of full doses of the drug. With administration of 1 Gm. of Diasone daily, blood levels were maintained between 1.5 and 2 mg. per hundred cubic centimeters. In a small group of cases, the concentration of "free" Diasone in the blood ranged from 1.7 to 2.5 mg., in the cerebrospinal fluid

178. Petter, C. K., and Prenzlau, W. S.: Observation on Clinical Application of Diasone in Human Tuberculosis (Eight Month Study), *Illinois M. J.* 85: 188-197 (April) 1944.

The technique does not use a bone graft in relation to a joint, and thus there is avoided friction of the bone against the articular condyles of the femur.

The operative procedure is relatively simple.

The re-establishing of the normal statics of the pelvis is accomplished by reversing the angulation of the metaphysis in a direction opposite to that of the acquired deformity and to approximately the same extent.

There is no disturbance of or interference with the musculature of the knee.

ED. NOTE.—I do not believe that Steinmann wires are necessary. Only one Kirschner wire is needed to maintain the upper fragment in extension. If a tongue of bone is left attached to the lower fragment, the second pin is not necessary and one is assured of good bone contact and good apposition of the fragments.

An important point that was not brought out is that genu recurvatum does not occur as a pelvic deformity; there is usually some genu valgum and external torsion as well as the recurvatum deformity. All three deformities can be corrected at one procedure if after completing the transverse osteotomy one rotates the distal fragment in such a manner that the external rotation, genu valgum and genu recurvatum are corrected and then with a Gigli saw removes the appropriate wedge of bone from the distal fragment, the sawed surface being parallel with the medial surface of the upper fragment. A description of this procedure can be found in *The Journal of the American Medical Association* for Sept. 1942.]

Mayer,<sup>253</sup> writing on the significance of the iliocostal fascial graft in the treatment of paralytic deformities of the trunk, describes three types of deformities being classified according to the underlying muscle imbalance. In the first, there is unilateral paralysis of all the muscles of the trunk. This produces a scoliosis with convexity on the paralyzed side and a downward tilt of the pelvis. This deformity leads to fixed pelvic obliquity. The second is due to the paralysis of the external and internal oblique muscles, but the quadratus lumborum muscle remains normal, so that there is no pelvic obliquity. In the third type there is paralysis of abdominal muscles on both sides, producing a downward tilt of the pelvis and an exaggerated lumbar lordosis. He states that these deformities are not always clear-cut but that two of these classifications may be present in one deformity. He stresses the im-

portance of early detection of these deformities followed by early treatment which comprises "well leg traction," pulling down on the elevated side of the pelvis and pushing up on the depressed side. This "well leg traction" may or may not be combined with a Risser type of turnbuckle jacket. He describes in detail the iliocostal fascial transplant which passes from the crest of the ilium to the ninth rib on the same side. Spinal fusion alone is not adequate to control these deformities, because if the muscle imbalance is allowed to remain the scoliosis will promptly recur. Spinal fusion, however, is an important part of the treatment in correcting the three types of deformities he describes with which there is an exaggerated lumbar lordosis. It is not clearcut when a spinal fusion or a fascial graft should be combined. His rule is to do the fascial graft first and observe the patient at three month intervals, and if the scoliosis increases as much as 10 degrees then a spinal fusion should be done. He reports 38 cases in which forty-six grafts were done. The results were good or excellent in 30 cases.

[ED. NOTE.—I cannot conceive of a fixed paralytic pelvic obliquity in the cases described under the first classification, wherein the deformity is confined to the trunk and can be corrected by fascial transplant alone. In these deformities the pelvis is not only oblique but displaced to one side. One must remember that a normal person when taking a step maintains the pelvis in a level position by the abductor muscles pulling down on the weight-bearing side, assisted by the lateral trunk groups pulling up on the opposite side, the femoral head being the fulcrum. When there is a paralysis of the trunk muscles on either side, this balanced system is disrupted. In all these cases there is a severe functional imbalance involving the side below the pelvic level on the side to which it is displaced and diagonally on the opposite side or trunk above the pelvic level. I have always done a Soutter fasciotomy to release the tight hip abductor muscles on the low side of the pelvis, followed by "well leg traction" in the attempt to restore the pelvis to its normal position. Then a fascial transplant is done on the same side. The pelvis cannot be restored to its original position in true fixed pelvic obliquity any more than one can completely correct the scoliosis with rotation. It is surprising how the walking of these persons is improved by simply doing a subtrochanteric osteotomy on the high side of the pelvis and shifting the femur nearer the midline.]

<sup>253</sup> Mayer, L.: The Significance of the Iliocostal Fascial Graft in the Treatment of Paralytic Deformities of the Trunk, *J. Bone & Joint Surg.* 26:257-271 (April) 1944.

length of the extremity should be made and an epiphysal arrest should be done in the opposite extremity at the appropriate time.

Mordasini<sup>194</sup> discusses the planogram as a valuable addition to the conventional roentgenograms in the diagnosis of tuberculosis in bone. A positive diagnosis can be made earlier. This technic is more useful in the frontal than in the lateral planes in tuberculosis of the spine. Case reports show that the early spinal lesion is not in the anterior part of the vertebra but that it starts in the central or the posterior portion of the body of the vertebra. Narrowing of the intervertebral spaces appears later.

[ED. NOTE.—The laminagraph has been proved to be of value in the detection of areas of tuberculosis of the vertebrae at the New York Orthopaedic Dispensary and Hospital.]

Meng and Wu<sup>195</sup> reviewed 70 cases of tuberculosis of flat bones of the vault, 40 of which had sufficient data for a definite diagnosis. Of the 40 cases, 20 were proved histologically and 5 by guinea pig inoculation or culture; 15 had sufficient clinical signs to justify the diagnosis. Eighty per cent of the patients were under 20 years of age. There were 23 men and 17 women. Trauma was not important or essential but may have been contributory. Eighty-five per cent had associated tuberculous lesions, and 50 per cent had pulmonary tuberculosis. Most lesions were, therefore, secondary hematogenous lesions starting in the diploe, and the tables were involved by extrusion. Two types of lesion are recognized: (a) the circumscribed (perforating) type of Volkmann (38 cases) and (b) the diffuse (infiltrating) type of Koenig (2 cases). There was a single lesion of the skull in 23 cases and multiple lesions in 17 cases. Most frequently involved were the frontal and the parietal bones because they contain a greater amount of cancellous bone. The onset was insidious, with only swelling evident. Pulsation of the mass indicates perforation of both tables. Differential diagnosis includes lipoma, sebaceous cyst, syphilis and

tumor. Results of roentgenologic examination are not typical and show only a round or oval single or a multiple punched-out defect. Aspiration is helpful. Treatment should be complete excision without drainage in the absence of a sinus, and the dura should be let alone. High voltage roentgen rays are sometimes of benefit.

Some of the causes of painful shoulder with radiation of the pain into the arm are discussed by Cohn.<sup>196</sup> No attempt is made to classify all the conditions which cause painful shoulder, but the diseases mentioned, with illustrative cases, are as follows: hypertrophic arthritis of the cervical portion of the spine, carcinoma metastasis to the cervical portion of the spine, herniated cervical intervertebral disk and tuberculosis of the cervical portion of the spine. The author also directs attention to these conditions which may be responsible for pain in the shoulder, i. e., cervical rib, the various neuritides and local lesions of the shoulder region, including arthritis, peri-arthritis, bursitis and tears of the supraspinatus tendon. A careful and detailed physical and roentgenographic examination is stressed as a necessary means of securing an accurate diagnosis.

The author observes that referred pain in tuberculosis of bones and joints is a common symptom, and any complaint referable to the shoulder, especially in the absence of definite physical abnormalities, should make one suspicious of a lesion of the cervical portion of the spine. Roentgenographic studies of the cervical portion of the spine should always be made in cases in which pain in the shoulder is the symptom, especially when local signs are absent, because not infrequently advanced changes will be noted on the roentgenogram even when the patient does not complain of symptoms referable to the neck. The author believes that the modus operandi of the referred pain in many cases of tuberculosis of the cervical portion of the spine is due to compression of the nerve roots by tuberculous granulation tissue. The referred pain, as a rule, promptly responds to immobilization of the cervical portion of the spine in a plaster cast.

196. Cohn, B. N. E.: Painful Shoulder Due to Lesions of Cervical Spine, *Am. J. Surg.* 66:269-274 (Nov.) 1944.

### VIII. CHRONIC ARTHRITIS

PREPARED BY JOHN G. KUHN, M.D., BOSTON

The appearance of arthritis and rheumatic fever in the armed forces has spurred further investigation and the development of special

services for their treatment. The newer antibiotic substances have been carefully studied in attempts to prevent or relieve these diseases.

194. Mordasini, E.: Beitrag zur Tomographie der Knochen und Gelenke unter besonderer Berücksichtigung der Knochen und Gelenktuberkulose, *Schweiz. med. Wchnschr.* 74:123 (Feb. 5) 1944.

195. Meng, C. M., and Wu, Y. K.: Tuberculosis of the Flat Bones of the Vault: Forty Cases, *Chinese M. J.* 61:155-171 (April-June) 1943.

In three papers by Rosenow,<sup>265</sup> the same idea about the Streptococcus is expanded and encephalitis is considered as a kindred entity to poliomyelitis. He calls attention to the fact that only streptococci with neurotrophic properties inherited or induced will yield "neurotrophic" virus. He suggests that the relation between the streptococci and the virus in encephalitis and poliomyelitis is phasal rather than synergistic. In most instances the streptococci were of the alpha type. He describes a cutaneous reaction, a precipitation test, results of agglutination procedures and the other qualities of immunity and antigen sensitivity.

Milzer and colleagues<sup>266</sup> report that the Lansing strain of virus is inactivated in less than the second's exposure to ultraviolet rays and that the inactivated virus could be used as a vaccine to prevent the disease in monkeys and mice.

[ED. NOTE (J. A. T.).—Before such a vaccine is tried, there is need for more and corroborative evidence.]

Meyer<sup>267</sup> believes that there is an inflammation of the walls of the jugular vein in patients with poliomyelitis, which responds promptly to the application of leeches over the inflamed jugular vein.

[ED. NOTE (J. A. T.).—There is no evidence to support this conception.]

Kramer, Geer and Szobel<sup>268</sup> tested the effects of innumerable agents for their viricidal activity—so far as barbiturates, dyes, organometallic compounds, sulfonamide compounds and a host of chemicals (one hundred and sixty items in all) were employed, with negative results.

[ED. NOTE (J. A. T.).—This is an important and fundamental piece of work.]

265. Rosenow, E. C.: Filterable Infectious Agent Obtained from Alpha Streptococci Isolated in Studies of Case of Poliomyelitis, *Am. J. Clin. Path.* **14**:519-533 (Oct.) 1944; Specific Streptococcal Antibody-Antigen Reactions in Poliomyelitis: Preliminary Report, *Proc. Staff Meet., Mayo Clin.* **19**:444-448 (Aug. 23) 1944; Studies on Virus Nature of Infectious Agent Obtained from Four Strains of "Neurotropic" Alpha Streptococci, *J. Nerv. & Ment. Dis.* **100**:229-262 (Sept.) 1944.

266. Milzer, A.; Oppenheimer, F., and Levinson, S. O.: Production of Potent Inactivated Vaccines with Ultraviolet Irradiation: Abbreviated Preliminary Report on Completely Inactivated Vaccine (Lansing Strain Virus) in Mice, *J. A. M. A.* **125**:704-705 (July 8) 1944.

267. Meyer, O.: New Principle in Treatment of Poliomyelitis, *Internat. Bull. M. Research & Pub. Hyg.* **A44**:P:5-9, 1944.

268. Kramer, S. D.; Geer, H. A., and Szobel, D. A.: Chemoprophylactic and Therapeutic Action of Wide Variety of Chemical Compounds on Two Neurotropic Virus Infections in Mice, *J. Immunol.* **49**:273-314 (Nov.) 1944.

Toomey<sup>269</sup> believes that sulfonamide compounds should not be given to patients with poliomyelitis, since experiments show an aggravation of the disease when these drugs are given to experimental animals.

Ehrlich and Foster<sup>270</sup> repeated histologic studies of mouse poliomyelitis and found it to be the same as that described by Lillie, Armstrong, Jungeblut and Sanders. There is good correlation between the histologic changes in the central nervous system and the clinical signs.

Jungeblut<sup>271</sup> showed that two strains of human poliomyelitis virus and Theiler's mouse encephalomyelitis virus revealed overlapping in cross neutralization and in antiviral immune serum tests, reciprocal in some but not so in others. He obtained evidence of group specificity after intracerebral tests and of strain specificity after intraperitoneal tests. He believes that all virus previously referred to could be classed under a "poliomyelitis group."

Paul<sup>272</sup> found that grivet and vervet monkeys are more susceptible to poliomyelitis virus than are baboons, and he feels that they are satisfactory animals to work with in experimental poliomyelitis.

Rasmussen and colleagues<sup>273</sup> showed that mice fed an adequate diet save for various levels of riboflavin showed no consistent differences to infection with Theiler's virus. In experiments with the Lansing strain, there was slight but definitely greater resistance in the deficient group.

McCormick<sup>274</sup> has for a long time been of the opinion that thiamine deficiency has something to do with poliomyelitis and that there is an affinity between beriberi and poliomyelitis.

Lichstein and co-workers<sup>275</sup> showed that mice fed rations deficient only in calcium pantothenate have increased resistance to Theiler's encephalitis but the course of the disease following infection with the Lansing virus is not influenced.

269. Toomey, J. A.: Treatment of Poliomyelitis, *J. A. M. A.* **126**:49 (Sept. 2) 1944.

270. Ehrlich, W. E., and Foster, C.: Experimental Poliomyelitis in Mice: Observations on Its Genesis and on Histologic Changes, *Arch. Path.* **38**:365-369 (Dec.) 1944.

271. Jungeblut, C. W.: Serologic Relationships Within Poliomyelitis Group of Viruses, *Am. J. Pub. Health* **34**:259-264 (March) 1944.

272. Paul, J. R.: Susceptibility of East African Monkeys to Experimental Poliomyelitis, *Yale J. Biol. & Med.* **16**:461-466 (May) 1944.

273. Rasmussen, A. F., Jr.; Waisman, H. A., and Lichstein, H. C.: Influence of Riboflavin on Susceptibility of Mice to Experimental Poliomyelitis, *Proc. Soc. Exper. Biol. & Med.* **57**:92-95 (Oct.) 1944.

(Footnotes continued on next page)



[ED. NOTE.—This is a well considered program for treatment in early rheumatic disease. Treatment cannot be standardized because of the multiplicity of possible causes and complicating factors, but a general outline such as this is helpful. Unfortunately, physicians now get patients late in their disease, when a long period of medical and surgical rehabilitation is required. It will probably require a long period of lay and professional education before this program can be applied effectively.]

In therapeutic attempts against chronic arthritis, the newer antibiotic substances have been used, with indifferent success. Boland and his collaborators<sup>215</sup> report on the use of penicillin in the treatment of active rheumatoid arthritis in an army hospital. In rheumatoid arthritis hemolytic streptococci have always been under suspicion. The blood usually contains antibodies against streptococci, usually agglutinins, in high titer. The skin is usually hypersensitive to extracts of hemolytic streptococci. Ten men were treated for whom the diagnosis of rheumatoid arthritis was definite and in whom the damage was not so severe that irreversible changes in the articular tissues had taken place. These patients were given 1,200,000 to 3,200,000 Oxford units daily. The penicillin was given every three hours for from fourteen to twenty days. There were no untoward reactions, and the changes observed were slight. In 8 patients there were no subjective or objective changes. One patient felt worse. In 1, slight subjective improvement was found. In 1, there was moderate subjective and objective improvement. Results of laboratory tests, including leukocyte count, sedimentation rate and cultures and smears for bacteria in the synovial fluid remained unchanged. The appetite improved in 6 of the 10 patients. The authors felt that penicillin was not of value in the treatment of rheumatoid arthritis.

Powell and Rice<sup>216</sup> used penicillin in treatment of rats which had arthritis caused by a pleuropneumonia-like organism. Treatment with penicillin was ineffective. Gold sodium thiomalate (Myocrysine) was effective in controlling the arthritis but was extremely toxic to the laboratory animals.

215. Boland, E. W.; Headley, N. E., and Hench, P. S.: Treatment of Rheumatoid Arthritis with Penicillin, *J. A. M. A.* **126**:820-823 (Nov. 25) 1944.

216. Powell, H. M., and Rice, R. M.: Ineffective Penicillin Chemotherapy of Arthritic Rats Infected with Pleuropneumonia-Like Organisms, *J. Lab. & Clin. Med.* **29**:372-374 (April) 1944.

Rawls<sup>217</sup> used small doses of gold thioglucose (Solgonal B oleosum), which contained 50 per cent gold, for 100 patients. Five milligrams was given twice a week for three weeks, 10 mg. twice a week for the next three weeks and then 25 mg. once a week. In 42 per cent of the patients toxic symptoms developed. Half of these occurred before 100 mg. of gold had been given. The patients quickly recovered from toxic symptoms in such small doses. The severity and duration of toxic symptoms depended on the dosage. There were no fatalities. In 53 per cent of the patients there was pronounced improvement, with almost complete remission of symptoms. Twenty-one per cent were definitely improved; 12 per cent were slightly improved.

Kennedy<sup>218</sup> used subcutaneous deposits of a sulfonamide compound in powder form in treatment of chronic infectious arthritis. He believes that in chronic rheumatoid arthritis the affected joints and lymph glands become metastatic septic foci. For these patients he uses a drachm (3.9 Gm.) or more of sulfanilamide powder subcutaneously in the affected limb. He states that improvement was observed in 3 chronic cases.

Neostigmine to relieve muscular spasm in rheumatoid arthritis was used by Trommer and Cohen<sup>219</sup> on 19 patients. One cubic centimeter of neostigmine methylsulfate (in a dilution of 1:2000) and 0.6 mg. of atropine sulfate were given every other day. In addition 7.5 to 45 mg. of neostigmine bromide with 0.6 to 1.2 cc. of tincture of belladonna were given daily. Thirteen patients showed decreased muscular spasm, and motions were carried out more readily. The effect following injection comes on in fifteen minutes and may last several days. [ED. NOTE.—The editor has observed the effect of neostigmine in similar dosage on a large number of patients during the past two years. Any beneficial effect observed was slight and transient. No lasting benefit was observed from its use.]

The chronically swollen, painful joint is one of the greatest problems in arthritis. Crowe<sup>220</sup>

217. Rawls, W. B., and others: Analysis of Results Obtained with Small Doses of Gold Salts in Treatment of Rheumatoid Arthritis, *Am. J. M. Sc.* **207**:528-533 (April) 1944.

218. Kennedy, R. T.: Chronic Infective Arthritis and an Experiment with Subcutaneous Deposits of Sulfonamide Powder, *M. J. Australia* **1**:150-152 (Feb. 19) 1944.

219. Trommer, P. R., and Cohen, A.: Neostigmine in the Treatment of Muscle Spasm in Arthritis and Associated Conditions, *J. A. M. A.* **124**:1237-1239 (April 29) 1944.

220. Crowe, H. W.: Treatment of Arthritis with Acid Potassium Phosphate, *Lancet* **1**:563-564 (April 29) 1944.

interference of a virus and thus upset cellular metabolism. The reported interference of poliomyelitis with the anaerobic glycolysis of the brain has not been confirmed.

Nickle and Kabat<sup>284</sup> claim some specific differences in metabolism between brain tissue infected with Western equine encephalomyelitis and that infected with poliomyelitis. Utilization of oxygen of the poliomyelitic brain is below normal with a glucose concentration of 121 mg. per hundred cubic centimeters; with a concentration of 217 mg. per hundred cubic centimeters utilization of oxygen of the encephalitic brain is below normal, but that of the poliomyelitic brain is not. Other substrates were used to show a difference, lactate-glucose, pyruvate-glucose and succinate-glucose.

Gellhorn<sup>285</sup> reports investigations on the influence of muscle pain on muscular incoordination. He concludes that movements are modified in intensity and equality not only by proprioceptive impulses but also by muscle pain.

Kabat and colleagues<sup>286</sup> report a decrease in lactic acid content of the brains of mice infected with poliomyelitis virus. They feel that this evidence supports the view that the virus does not interfere with metabolism.

Carey's publication<sup>287</sup> is fundamental and describes the early histologic changes that occur in the neuromuscular mechanism of experimental poliomyelitis in monkeys. The early loss of the motor end plate was striking. He suggests tentatively that the changes are a result of abnormal excitation of the secretory mechanism of the motor end plates which results in progressive exhaustion of the gold-staining axonic substance leading to denervation at the myoneural junction. Gard<sup>288</sup> describes two colonies of albino mice in which, during epizootics caused by *Salmonella enteritidis* and *Bacillus piliformis*, there were 10 and 5 cases of spontaneous mouse poliomyelitis observed. The transfers were easiest when made from the intestine, next easiest from the lymph nodes and then from the tissue of the

central nervous system. The involvement of the lymph node was stressed.

Herrarte and Francis<sup>289</sup> described several methods of recovering virus from various biologic specimens.

Bourdillon<sup>290</sup> studied the sedimentation, the electrophoretic mobility and the serologic reactivity of purified Jungeblut's SK adapted mouse strain in its two hundred and seventieth to three hundred and twentieth passage. The injected dose was always 0.03 cc. of serial dilutions.

[ED. NOTE (J. A. T.).—The article is a technical one; suffice it to say that it is one not well suited for abstract.]

Foster and Ehrich<sup>291</sup> describe the technics which they used to demonstrate the alterations of brain and spinal cord characterizing infection with Lansing strain of virus in the mouse.

Bourdillon<sup>292</sup> describes in detail the methods of purification of virus by means of the Swedish angle centrifuge.

A long article on the therapy of poliomyelitis in the acute stages of the disease has been written by Toomey.<sup>293</sup> He concludes:

1. As first shown by Feiss, immobilization and splints are unnecessary in the acute stages of poliomyelitis.
2. Active movement, manipulations, etc., in the acute stage of the disease do not harm the patient.
3. Some form of heat should be used to bring about vascular dilatation in the early stages of the disease. The muscles should be moved through their normal arcs.
4. Muscle reeducation plays the most important role in poliomyelitis therapy. It should be started early and should be persistently carried out over a long period of time.

An excellent article by Ward<sup>294</sup> is devoted to the epidemiology of poliomyelitis. He gives a good review of the probable epidemiologic facts known to date.

284. Nickle, M., and Kabat, H.: Specificity in Effects of Brain Metabolism of Two Differing Neurotropic Viruses, *J. Exper. Med.* **80**:247-255 (Sept.) 1944.

285. Gellhorn, E.: Effect of Muscle Pain on Central Nervous System at Spinal and Cortical Levels, *Journal of Neurology* **64**:242-245 (July) 1944.

286. Kabat, H.; Erickson, D.; Eklund, C., and Nickle, M.: Decrease in Lactic Acid Content of Brain in Poliomyelitis, *Science* **98**:589-591 (Dec. 31) 1943.

287. Carey, E. J.: Study on Ameboid Motion and Secretion of Motor End-Plates: Anatomic Effects of Poliomyelitis of Neuromuscular Mechanism in Monkey, *m. J. Path.* **20**:961-995 (Sept.) 1944.

288. Gard, S.: Observations Concerning the Pathogenesis and the Epidemiology of Mouse Poliomyelitis, *Am. J. Biol. & Med.* **16**:467-476 (May) 1944.

289. Herrarte, E., and Francis, T., Jr.: Efforts Toward Selective Extraction of Poliomyelitis Virus, *J. Infect. Dis.* **73**:206-211 (Nov.-Dec.) 1943.

290. Bourdillon, J.: Purification, Sedimentation, and Serological Reactions of the Murine Strain of SK Poliomyelitis Virus, *Arch. Biochem.* **3**:285-297 (Feb.) 1944.

291. Foster, C., and Ehrich, W. E.: Demonstration of Lesion Produced by Experimental Poliomyelitis in Central Nervous System of Mouse, *Arch. Path.* **37**:264-271 (April) 1944.

292. Bourdillon, J.: Heat Inactivation of Murine Strain of SK Poliomyelitis Virus, *Arch. Biochem.* **3**:299-303 (Feb.) 1944.

293. Toomey, J. A.: Observations on Treatment of Infantile Paralysis in Acute Stage (Nathan Lewis Hatfield Lecture), *Tr. & Stud., Coll. Physicians, Philadelphia* **12**:14-25 (April) 1944.

294. Ward, R.: The Epidemiology of Poliomyelitis, *J. Bone & Joint Surg.* **26**:829-832 (Oct.) 1944.

us organic matter survives more than ten times this amount of residual chlorine.

Arguments against flies playing a role in transmission are as follows: 1. Flies are not invariably associated with the disease, as in winter poliomyelitis. 2. The disease would not attack children preponderantly, as is the case, if it were transmitted primarily by the fly or any other insect. One would expect just such a high incidence in children if adults were immune because of infection—preponderantly abortive or non-paralytic—acquired in childhood or immunity acquired by other, as yet unrecognized, means.

The probability of obtaining virus from flies trapped in epidemic areas would appear to be as good as that of obtaining it from stools and certainly better than that of finding it in nasopharyngeal washings.

Contact infection is admittedly a means of spread, but that it is "the most important means" has not been proved to the authors' satisfaction. Seasonal incidence cannot be explained in this way (epidemics fade out when school opens). The rarity of hospital infection from patient to patient and from patient to hospital personnel would militate against the philosophy of greater segregation as a solution, or even as an aid to a solution, to the problem.

The authors express the belief that it is wise to keep receptive minds to evidence which may eventually show other "modes of spread of infantile paralysis," more in keeping with present knowledge of the natural history of the disease.

Horstmann, Ward and Melnick<sup>235</sup> undertook a study to determine the average duration of excretion of virus in stools of patients following acute infection and to ascertain whether a chronic carrier state similar to that occurring in typhoid exists in poliomyelitis. The stools of 61 patients (46 paralytic and 15 nonparalytic) were collected during the first or second week of the disease and at four to six week intervals thereafter. The materials collected were frozen immediately or within a few hours after collection and stored on solid carbon dioxide until ready to be tested. The inoculum (prepared by Melnick's technic with a few minor changes) was ultracentrifuged at 39,000 revolutions per minute and inoculated into immature rhesus monkeys, by the intracerebral route in fifty-four tests, directly into the lumbar portion of the cord in eighty tests and by a combination of the two routes in twelve. All but 2 monkeys were ultimately killed, and the result of a test

considered positive when microscopic lesions characteristic of poliomyelitis were seen in the spinal cord. It was found that 61 per cent of the patients excreted virus during the first two weeks after onset of the disease, 50 per cent during the third and fourth weeks, 27 per cent during the fifth and sixth weeks and 12.5 per cent during the seventh and eighth weeks. Between the ninth and twenty-fourth weeks, virus was detected in only 1 of 52 specimens tested, 1 patient excreting it in the twelfth week. Not one of the 61 patients followed was demonstrated to become a persistent carrier of poliomyelitis virus.

Maxcy<sup>236</sup> states that present day conceptions of epidemiology of poliomyelitis rest in a large part on the observations made in Norway and Sweden toward the end of the nineteenth century and during the early part of this century, which are available in the classic monograph of Ivan Wickman, published in English translation in 1913. Studies in the United States began with the reports of Dr. Charles S. Caverley on the occurrence of anterior poliomyelitis in the state of Vermont in 1894 and were continued by Flexner and Lewis after the 1907 epidemic in New York and by W. H. Frost after the 1910 outbreak in Minnesota and Nebraska, the 1911 occurrence in Iowa, the outbreak in Cincinnati in 1911 and in Buffalo and Batavia, N. Y., in 1912. The largest epidemic which this country has experienced occurred in and about the city of New York in 1916 and was studied in great detail by three officers of the United States Public Health Service. C. H. Lavinder, A. W. Freeman and W. H. Frost. Since the publication of their report, the large number of contributions from investigators in this country and abroad have served to confirm, amplify and extend the basic observations, although the net advance has been relatively small.

After review of available morbidity and mortality data, with considerations of their limitations in mind, the following brief interpretations regarding broad general characteristics appear to be valid:

1. The disease is worldwide in distribution.
2. From no human community is the disease long absent.
3. Transmission can occur in any month of the year.

235. Horstmann, D. M.; Ward, R., and Melnick, J. L.: Persistence of Virus Excretion in the Stools of Poliomyelitis Patients, *J. A. M. A.* **126**:1061-1062 (Dec. 23) 1944.

236. Maxcy, K. F.: A Review of the Epidemiology of Acute Anterior Poliomyelitis with Reference to the Mode of Transmission, *Journal-Lancet* **64**:216-223 (July) 1944.

involved segments by immobilization in splints or casts in a neutral position during the stage of tenderness or contracture. In order to prevent stiffness, the splints and casts are removed once or twice a day and the joints moved passively through as great an arc as can be tolerated by the patient. In the convalescent stage, splints or casts are removed and the patient is encouraged to move about in bed and exercise his limbs in order to loosen up the muscles and joints. Once or twice a day he is placed in a tub of warm water and the paralyzed limbs are exercised. Muscle training preferably is carried out by skilled physical therapists, but the mother or a nurse may be taught to carry on the prescribed treatment for a given patient in a satisfactory manner. In the chronic stage, orthopedic apparatus is used to prevent deformities and improve function of paralyzed segments. Key states:

This is the orthodox treatment and when it is properly carried out approximately 80 per cent of the patients who develop infantile paralysis during an epidemic may be expected to recover to a point at which they are normal or practically normal. About 20 per cent will be crippled permanently to a variable degree, but only about 1 per cent will be crippled so severely that they will become wheel chair cases.

These figures are from three recent epidemics. Key also states that he does not approve of the Kenny method and enumerates sixteen reasons why he does not.

Scott and Rountree<sup>299</sup> report on 46 cases which occurred during the period from March to November 1941. Thirty-nine patients had or contracted paralysis shortly after admission to the hospital. Thomas splints and Bradford frames were used for all patients. At the end of two years, accurate follow-up studies were made on 39 of the 46 patients. There were 3 (7.7 per cent) deaths. Nine patients (23 per cent) made a complete recovery. Twelve (30.7 per cent) were released from treatment, and 15 (38.4 per cent) were still under treatment. Of the 12 released from treatment, 7 were able to walk without appliances, 3 were able to walk with appliances and 2 were unable to walk. Of the 15 still under treatment, 8 were able to walk without appliances and 3 with appliances and 4 were unable to walk. "The results of the treatments used are not encouraging."

*Kenny Method of Treatment.*—O'Connor<sup>300</sup> gives the history of the Kenny method, out-

lining the aid given to Kenny by the National Foundation for Infantile Paralysis, Inc.

Kenny<sup>301</sup> presents and answers two questions: first, concerning her concept of the disease, acute anterior poliomyelitis, and second, concerning the treatment for this concept. As evidence of the value of her treatment over "orthodox treatment," she presents first the report of McCarroll (*J. A. M. A.* 120:517-519 [Oct. 17] 1942) and contrasts this report with that of Bingham (*J. Bone & Joint Surg.* 25: 647-650 [July] 1943). Kenny feels that her answers given in the latter article substantiate the claim that her contribution is not a treatment for recognized symptoms but an entirely new concept of the disease itself.

Knapp<sup>302</sup> presents his observations on the symptoms and treatment of poliomyelitis. He makes the statement that "Muscle shortening is a positive entity in infantile paralysis and is an important factor in the final function end-result." He states that "'mental alienation' is probably only a minor factor in infantile paralysis and is probably not psychologic in origin as thought by Miss Kenny." Maximum efficiency of muscle function within the limits imposed on it by denervation is the aim of treatment and the explanation for the good results obtained.

[ED. NOTE.—Dr. Knapp in this article presents his own opinion of the symptoms and treatment. It is worth while to read of this treatment and the article of Kenny mentioned. As is well known, Kenny and Knapp have worked together since Kenny's first visit to the United States, in 1940.]

Ghormley and colleagues<sup>303</sup> present a report of the committee for the investigation of the Kenny treatment of poliomyelitis, following a resolution passed by the Section on Orthopedic Surgery of the American Medical Association. This committee visited a total of six cities and sixteen clinics. A total of approximately 740 patients were examined. Approximately 650 of these patients had been treated by the method advocated by Miss Kenny. The report discusses four major points of the concept of the disease and outlines the major points of the Kenny treatment. Each of the points outlined was

301. Kenny, E.: *Kenny Treatment of Poliomyelitis*. Proc. Interst. Postgrad. M. A. North America (1942). 1943, pp. 312-316.

302. Knapp, M. E.: *Observations on Infantile Paralysis*, *Journal-Lancet* 64:164-168 (May) 1944.

303. Ghormley, R. K., and others: *Evaluation of the Kenny Treatment of Infantile Paralysis*, *J. A. M. A.* 125:466-469 (June 17) 1944; *Evaluation of the Kenny Treatment of Infantile Paralysis*, *Arch. Phys. Therapy* 25:415-420 (July) 1944.

299. Scott, E. B., and Rountree, G. R.: *A Study of Forty-Six Cases of Poliomyelitis*, *Kentucky M. J.* 42: 182-184 (June) 1944.

300. O'Connor, B.: *The Story of the Kenny Method*, *Arch. Phys. Therapy* 25:231-234 (April) 1944.

to simulate other disease. The critical findings of differential diagnostic value depend on signs of cord, brain and nerve irritation and must be supported by physical findings. These are sometimes so extremely variable and changeable that they may be detected only by careful, deliberate and repeated examinations. The most important sign is nuchal rigidity, which is accompanied with or followed by spinal tenderness. Kernig's sign may appear early or not. Deep reflexes are present but variable (hyperactive to sluggish). The muscle groups or muscles presenting tremors are likely to be involved. Rigidity of muscles, deep tenderness, discrete areas of perspiration, irritation of rectal or vesical centers in the lumbar part of the cord, with resulting constipation or urine retention, all may be demonstrated. Bulbar involvement may have a rapid onset, with difficulty in swallowing, impairment of phonation, salivation and excessive mucous secretion, disorientation, delirium and coma.

Puncture of the lumbar part of the cord is of therapeutic value in reducing intracranial pressure. The spinal fluid is normal throughout the first febrile and asymptomatic stages of the disease. At the onset of the paralytic phase, the spinal fluid is clear, there is increased pressure, the cells may vary from 10 to 200, the total protein is increased and the fluid is sterile on bacteriologic examination and does not contain the virus. Hence, examination of the spinal fluid is important if the results are positive but not necessarily contradictory when values are normal. The blood count and sedimentation rate are not contributory to diagnosis. Differential diagnosis is important in acute poliomyelitis to rule out purulent meningitis, encephalitis, St. Louis encephalitis and occasionally acute arthritis. The cardinal points of early diagnosis are: (1) awareness of poliomyelitis, (2) history of febrile attack a few days previously, (3) headache and fever, (4) nuchal rigidity and spinal tenderness, (5) spasm, tremor or weakness in a muscle or muscle groups, (6) hyperesthesia or pain, (7) reflex changes and (8) cerebrospinal fluid changes if positive. The author states that (9) the serious grade of the disease is indicated by progressive course and that (10) it is impossible to diagnose subclinical cases in the acute stage.

*Prevention.*—Lumsden,<sup>242</sup> in writing on the epidemiology of poliomyelitis and measures for its prevention, states that the possibility of sev-

eral specific viruses of poliomyelitis is given weight by the fact that strains of the virus obtained in different outbreaks present pronounced differences biologically, serologically, immunologically and otherwise. There are many possible modes of transmission, but none are conclusive. Preventive measures suggested are: (1) cleanliness and maintenance of cleanliness (hygiene and sanitation); (2) systematic, intense and continuous fights on rats, mice, flies, mosquitoes, roaches, fleas, bedbugs, ants, insects and vermin; (3) strict sanitation regarding disposal of garbage, manure and excreta of poultry and birds; (4) screening of living and sleeping quarters; (5) purified water supplies and sanitary sewage systems with final disposal; (6) rigid sanitary and hygienic supervision of public eating and drinking places; (7) educational campaign to discourage potential droplet infection (coughing, sneezing, spitting, blowing and wiping); (8) reasonable discouraging of public assemblages by children under 6 years, and (9) restraining of young children from undue physical stress. Closing of schools, churches and theaters, as is often demanded by misled public opinion, is unjustified; placarding of the affected homes is advisable; proper isolation of patients is advisable to guard against superimposed infections. There should be rigid disinfection of discharges from nose and mouth and feces. Quarantine is not justified except for food handlers and persons in close contact with large numbers of children.

*Pathology.*—Dublin, Bede and Brown<sup>243</sup> report their findings on studies of muscles taken for biopsy from 3 patients with poliomyelitis and stained by the Ranvier method. They observed a degeneration of nerve fibers, motor end plates and muscle fibers in a degree commensurate with the degree of paralysis; an irregularity of distribution in keeping with an irregularity of distribution of injury to nerve cells of the gray matter of the spinal cord; a degeneration of nerve fibers, consisting largely in failure of axons to stain together with preservation of cellular elements of capsules of motor endings and of sheaths of Schwann; atrophy of muscle fibers appearing as pyknosis, beginning with loss of cross striations and increase of longitudinal markings; degeneration of muscle and nerve ranking probably secondary to injury to nerve cells of the spinal cord, and no definite evidence of activity of degeneration or regeneration.

242. Lumsden, L. L.: Poliomyelitis: Its Epidemiology and Measures for Its Prevention. Texas Rep. Biol. & Med. 1:233-241, 1943.

243. Dublin, W. B.; Bede, B. A., and Brown, B. A.: Pathologic Findings in Nerve and Muscle in Poliomyelitis. Am. J. Clin. Path. 14:266-272 (May) 1944.

and Kenny technic. Of the 21 cases, there were added to excellent end results in all. The modification of the Kenny technic consisted in the elimination of hot packs and the substitution of atropine, usually orally but occasionally parenterally as well. No change was made in the usual methods of muscle reeducation of or in the passive joint movement procedure. He states, "Approximately 75 per cent of patients with poliomyelitis can be adequately cared for at home without special nursing attention with this technique." Boines also urges the extension of this method of therapy especially in chronic cases. McFarland and colleagues<sup>312</sup> make a preliminary report of a series of 74 selected cases in which neurotripty was combined with the Kenny treatment. In 25 of these cases neurotripty was given while the Kenny treatment was being given in the acute stage, and in 49 cases of longstanding residual paresis neurotripty also was given in combination with the Kenny method. The rationale of neurotripty is the fact that in regrowth after nerve interruption there is an increased branching. The authors present an outline of the procedure, which is done with general or spinal anesthesia with the objective of breaking as many branches of the remaining motor nerve axons as possible. The technic is to knead through the muscle vigorously and deeply with a blunt instrument. The muscle is covered thoroughly throughout its entire extent. There has been a rather consistent increase in circulation in the involved segments, and an increase in muscle size is a "frequent result." Improvement in muscle strength occurred in over one half of one hundred and thirty muscle groups studied. "The results are encouraging."

Miley<sup>313</sup> presents a preliminary report on 38 cases in which the Knott technic of ultraviolet irradiation of blood was used in addition to the Kenny treatment. There were no harmful effects in this series of cases. This technic did not interfere with the Kenny routines. No attempt was made to evaluate the ultimate end results for these patients, but it is Miley's conclusion that further extensive clinical studies with this combination of treatments is warranted.

Nelson<sup>314</sup> discusses the present status of poliomyelitis. Regarding treatment, he says that hot

packs during the stage of spasm followed by muscle reeducation offer the most help in the acute stages.

Compere<sup>315</sup> outlines the management and care of patients with infantile paralysis. He states that his own observation led to the conclusion that the earlier the program of treatment of peripheral manifestations is done the better are the end results. Microscopic sections of muscles that are in spasm show a picture of pathologic congestion. This congestion may be relieved by hot packs, passive motion and active exercise. He further concludes that the number of patients who will require surgical intervention may be as large as that of the patients who have received other types of treatment but that the patients given treatment by hot packing, early activity, exercises and good physical therapy will be in better condition generally and will thus obtain greater profit from the efforts of the orthopedic surgeon.

Wright<sup>316</sup> presents problems encountered in the early treatment of poliomyelitis. She states that Kenny has made a valuable contribution but that one will continue to use to advantage the Silver method of the prevention of stasis of the circulation by special postural measures in bed, the Lovett-Merrill method of muscle testing, the Kendall percentage grading, the Lowman under water reeducation and the light, efficient supports when indicated. In a second article, Wright<sup>317</sup> outlines a reasonable program of treatment for acute poliomyelitis. She notes that "treatment can not be by one method only but must meet the needs of each case."

Wolf<sup>318</sup> in discussing the clinical aspects of poliomyelitis, states that "when a patient with pure bulbar poliomyelitis is placed in a respirator it can be seen that more harm than good results. The patient breathes with the machine at times and against it at others. The use of the respirator under these conditions may be extremely harmful."

Thompson<sup>319</sup> discusses the Kenny method and correlates a program of occupational therapy combined with the Kenny method.

315. Compere, E. L.: Management and Care of the Infantile Paralysis Patient, *Arch. Phys. Therapy* **24**: 709-712 (Dec.) 1943.

316. Wright, J.: Problems in Early Treatment of Poliomyelitis, *New York State J. Med.* **44**:67-72 (Jan. 1) 1944.

317. Wright, J.: Reasonable Treatment of Acute Poliomyelitis, *Pub. Health Nursing* **36**:510-515 (Oct.) 1944.

318. Wolf, A. M.: Symposium on the Management of Poliomyelitis, *Am. J. Dis. Child.* **67**:332-334 (April) 1944.

(Footnotes continued on next page)

312. McFarland, J. W.; Billig, H. E., Jr.; Taylor, G. M., and Dail, C. W.: Kenny Treatment Combined with Neurotripty in Care of Poliomyelitis, *Arch. Phys. Therapy* **25**:645-650 (Nov.) 1944.

313. Miley, G.: Ultraviolet Blood Irradiation Therapy in Acute Poliomyelitis, *Arch. Phys. Therapy* **25**: 651-656 (Nov.) 1944.

314. Nelson, N. B.: Poliomyelitis: Its Present Status, *California & West. Med.* **60**:18-21 (Jan.) 1944.

3. The technique does not use a bone graft in relation to the joint, and thus there is avoided friction of the joint against the articular condyles of the femur.
4. The operative procedure is relatively simple.
5. The re-establishing of the normal statics of the knee is accomplished by reversing the angulation of the metaphysis in a direction opposite to that of the acquired deformity and to approximately the same degree.
6. There is no disturbance of or interference with the musculature of the knee.

[ED. NOTE.—I do not believe that Steinmann pins are necessary. Only one Kirschner wire is needed to maintain the upper fragment in hyperextension. If a tongue of bone is left attached to the lower fragment, the second pin is not necessary and one is assured of good bone contact and good apposition of the fragments. One important point that was not brought out is that genu recurvatum does not occur as a single deformity; there is usually some genu valgum and external torsion as well as the recurvatum deformity. All three deformities can be corrected at one procedure if after completing the transverse osteotomy one rotates the distal fragment in such a manner that the external torsion, genu valgum and genu recurvatum are corrected and then with a Gigli saw removes the appropriate wedge of bone from the distal fragment, the sawed surface being parallel with the cut surface of the upper fragment. A description of this procedure can be found in *The Journal of the American Medical Association* for Sept. 26, 1942.]

Mayer,<sup>253</sup> writing on the significance of the iliocostal fascial graft in the treatment of paralytic deformities of the trunk, describes three types. The deformities being classified according to the underlying muscle imbalance. In the first, there is a unilateral paralysis of all the muscles of the trunk. This produces a scoliosis with convexity to the paralyzed side and a downward tilt of the pelvis. This deformity leads to fixed pelvic obliquity. The second is due to the paralysis of external and internal oblique muscles, but the quadratus lumborum muscle remains normal, so that there is no pelvic obliquity. In the third type there is paralysis of abdominal muscles on both sides, producing a downward tilt of the pelvis and an exaggerated lumbar lordosis. He states that these deformities are not always clear-cut but that two of these classifications may be present in one deformity. He stresses the im-

portance of early detection of these deformities followed by early treatment which comprises "well leg traction," pulling down on the elevated side of the pelvis and pushing up on the depressed side. This "well leg traction" may or may not be combined with a Risser type of turnbuckle jacket. He describes in detail the iliocostal fascial transplant which passes from the crest of the ilium to the ninth rib on the same side. Spinal fusion alone is not adequate to control these deformities, because if the muscle imbalance is allowed to remain the scoliosis will promptly recur. Spinal fusion, however, is an important part of the treatment in correcting the three types of deformities he describes with which there is an exaggerated lumbar lordosis. It is not clearcut when a spinal fusion or a fascial graft should be combined. His rule is to do the fascial graft first and observe the patient at three month intervals, and if the scoliosis increases as much as 10 degrees then a spinal fusion should be done. He reports 38 cases in which forty-six grafts were done. The results were good or excellent in 30 cases.

[ED. NOTE.—I cannot conceive of a fixed paralytic pelvic obliquity in the cases described under the first classification, wherein the deformity is confined to the trunk and can be corrected by fascial transplant alone. In these deformities the pelvis is not only oblique but displaced to one side. One must remember that a normal person when taking a step maintains the pelvis in a level position by the abductor muscles pulling down on the weight-bearing side, assisted by the lateral trunk groups pulling up on the opposite side, the femoral head being the fulcrum. When there is a paralysis of the trunk muscles on either side, this balanced system is disrupted. In all these cases there is a severe functional imbalance involving the side below the pelvic level on the side to which it is displaced and diagonally on the opposite side or trunk above the pelvic level. I have always done a Soutter fasciotomy to release the tight hip abductor muscles on the low side of the pelvis, followed by "well leg traction" in the attempt to restore the pelvis to its normal position. Then a fascial transplant is done on the same side. The pelvis cannot be restored to its original position in true fixed pelvic obliquity any more than one can completely correct the scoliosis with rotation. It is surprising how the walking of these persons is improved by simply doing a subtrochanteric osteotomy on the high side of the pelvis and shifting the femur nearer the midline.]

253. Mayer, L.: The Significance of the Iliocostal Fascial Graft in the Treatment of Paralytic Deformities of the Trunk, *J. Bone & Joint Surg.* 26:257-271 (April) 1944.

occupation; 14 per cent obtained good results but have not yet returned to normal activity; 14 per cent obtained fair results, with no complete paralysis but with definite weakness, and 22 per cent had a residual definite loss of one or more muscle groups.

Poehler<sup>329</sup> outlines an ideal set-up for the treatment of poliomyelitis following the remodeling of "Sheltering Arms" in Minneapolis. She stresses the fact that patients during the convalescent stage of poliomyelitis are not sick in

329. Poehler, J. A.: Remodeled for "Polio" Patients. *Mod. Hosp.* 62:58-60 (Jan.) 1944.

the sense that the word is usually understood and should not be treated in hospitals planned and maintained for acutely ill persons.

Gudakunst<sup>330</sup> discusses the problem of infantile paralysis, setting forth the gains made in the handling and treatment of patients. He brings out the purpose and scope of the work of The National Foundation for Infantile Paralysis, Inc.

330. Gudakunst, D. W.: Fighting Infantile Paralysis, Survey 80:254-256 (Sept.) 1944; Facing the Future in the Fight Against Infantile Paralysis, *J. Health & Phys. Educ.* 15: 258 (May) 1944.

## NII. NEUROMUSCULAR DISORDERS EXCLUSIVE OF POLIOMYELITIS

PREPARED BY WINTHROP M. PHELPS, M.D., BALTIMORE

During 1943 there was an increase in the volume of literature dealing with neuromuscular disorders. This is especially interesting in view of the pronounced decrease of the year before. The distribution of the material has changed only slightly. That referring to cerebral palsy has increased the most, and the articles on peripheral paralysis and surgery are close seconds. The papers dealing with pure research in the field are still scarce.

The material can be considered under nine chief headings, which are as follows: (1) cerebral palsy, (2) peripheral paralysis, (3) myopathies, (4) ataxia, (5) neuralgia, (6) diagnostic procedures, (7) surgery, (8) vitamins and (9) drugs.

*Cerebral Palsy.*—A paper by Lucksch<sup>331</sup> describes 2 cases, brought to autopsy, of the disease previously called "cerebral infantile paralysis." Lucksch suggests that the designation be changed to "encephalopathia infantum." The change, he feels, is more descriptive of conditions observed and yet is not specifically a description of a disease entity. [ED. NOTE.—This is an anatomic title whereas the usual term "cerebral palsy" is a descriptive one, and the latter, of course, is much more in keeping with American custom.]

Yannet<sup>332</sup> has written an interesting paper on the study of 86 patients with cerebral palsy. He notes that the average age of the mother at the time of birth of the affected child is greater than that found in the general population. The affected children tend to have a later ordinal

birth rank than would be normally expected. [ED. NOTE.—This might be expected in view of the recent observations in regard to the Rh factor.] He also finds that the incidence of mental deficiency in the nonaffected siblings is greater than would be expected from random selection. He finds an unusually high incidence of associated physical defects, especially those involving the eyes. [ED. NOTE.—In my experience, this is also true of hearing defects.] Yannet feels that this points to the importance of developmental cerebral malformations in the causation of cerebral palsy.

Phelps<sup>333</sup> describes the treatment of various types of cerebral palsy in some detail and emphasizes the need for proper classification of the individual cases in order to carry out differential treatment.

Salisbury<sup>334</sup> draws attention to the increased interest in cerebral palsy throughout the country and the greater number of cases encountered in the clinics and in private practice and emphasizes the great need for a national foundation for this condition, since it is as frequent in distribution as poliomyelitis.

Arieff and Kaplan<sup>335</sup> describe cerebellar ataxia associated with cerebral signs. This is, of course, not commonly seen, but it is well to bear in mind the complications of neurologic changes which may occur.

Welch and Kennard<sup>336</sup> describe flaccid paralysis in relation to the cerebral cortex. This is

333. Phelps, W. M.: Symposium on Orthopaedic Surgery: Treatment of Cerebral Palsies, *Clinics* 2:981-991 (Dec.) 1943.

334. Salisbury, P. A.: Needed—National Foundation for Cerebral Palsy, *Hospitals* 18:50-53 (April) 1944.

335. Arieff, A. J., and Kaplan, L. A.: Cerebellar Type of Ataxia Associated with Cerebral Signs, *J. Nerv. & Ment. Dis.* 100:135-141 (Aug.) 1944.

(Footnotes continued on next page)

331. Lucksch, F.: Description of Two Autopsy Cases of "Cerebral Infantile Paralysis," with Suggestion for Changing Designation to "Encephalopathia Infantum," *Psychiat.-neurol. Wchnschr.* 45:137 (May 22) 1943.

332. Yannet, H.: Etiology of Congenital Palsy: Statistical and Clinical Study, *J. Pediat.* 24:38-45 (Jan.) 1944.



by interference of a virus and thus upset cellular metabolism. The reported interference of poliomyelitis with the anaerobic glycolysis of the brain has not been confirmed.

Nickle and Kabat<sup>284</sup> claim some specific differences in metabolism between brain tissue infected with Western equine encephalomyelitis and that infected with poliomyelitis. Utilization of oxygen of the poliomyelitic brain is below normal with a glucose concentration of 121 mg. per hundred cubic centimeters; with a concentration of 217 mg. per hundred cubic centimeters utilization of oxygen of the encephalitic brain is below normal, but that of the poliomyelitic brain is not. Other substrates were used to show a difference, lactate-glucose, pyruvate-glucose and succinate-glucose.

Gellhorn<sup>285</sup> reports investigations on the influence of muscle pain on muscular incoordination. He concludes that movements are modified in intensity and equality not only by proprioceptive impulses but also by muscle pain.

Kabat and colleagues<sup>286</sup> report a decrease in the lactic acid content of the brains of mice infected with poliomyelitis virus. They feel that this evidence supports the view that the virus may interfere with metabolism.

Carey's publication<sup>287</sup> is fundamental and describes the early histologic changes that occur in the neuromuscular mechanism of experimental poliomyelitis in monkeys. The early loss of the motor end plate was striking. He suggests tentatively that the changes are a result of abnormal excitation of the secretory mechanism of motor end plates which results in progressive exhaustion of the gold-staining axonic substance leading to denervation at the myoneural junction.

Gard<sup>288</sup> describes two colonies of albino mice in which, during epizootics caused by *Salmonella enteritidis* and *Bacillus piliformis*, there were 4 and 5 cases of spontaneous mouse poliomyelitis observed. The transfers were easiest when made from the intestine, next easiest from the lymph nodes and then from the tissue of the

central nervous system. The involvement of the lymph node was stressed.

Herrarte and Francis<sup>289</sup> described several methods of recovering virus from various biologic specimens.

Bourdillon<sup>290</sup> studied the sedimentation, the electrophoretic mobility and the serologic reactivity of purified Jungeblut's SK adapted mouse strain in its two hundred and seventieth to three hundred and twentieth passage. The injected dose was always 0.03 cc. of serial dilutions.

[ED. NOTE (J. A. T.).—The article is a technical one; suffice it to say that it is one not well suited for abstract.]

Foster and Ehrich<sup>291</sup> describe the technics which they used to demonstrate the alterations of brain and spinal cord characterizing infection with Lansing strain of virus in the mouse.

Bourdillon<sup>292</sup> describes in detail the methods of purification of virus by means of the Swedish angle centrifuge.

A long article on the therapy of poliomyelitis in the acute stages of the disease has been written by Toomey.<sup>293</sup> He concludes:

1. As first shown by Feiss, immobilization and splints are unnecessary in the acute stages of poliomyelitis.

2. Active movement, manipulations, etc., in the acute stage of the disease do not harm the patient.

3. Some form of heat should be used to bring about vascular dilatation in the early stages of the disease. The muscles should be moved through their normal arcs.

4. Muscle reeducation plays the most important role in poliomyelitis therapy. It should be started early and should be persistently carried out over a long period of time.

An excellent article by Ward<sup>294</sup> is devoted to the epidemiology of poliomyelitis. He gives a good review of the probable epidemiologic facts known to date.

289. Herrarte, E., and Francis, T., Jr.: Efforts Toward Selective Extraction of Poliomyelitis Virus, *J. Infect. Dis.* **73**:206-211 (Nov.-Dec.) 1943.

290. Bourdillon, J.: Purification, Sedimentation, and Serological Reactions of the Murine Strain of SK Poliomyelitis Virus, *Arch. Biochem.* **3**:285-297 (Feb.) 1944.

291. Foster, C., and Ehrich, W. E.: Demonstration of Lesion Produced by Experimental Poliomyelitis in Central Nervous System of Mouse, *Arch. Path.* **37**:264-271 (April) 1944.

292. Bourdillon, J.: Heat Inactivation of Murine Strain of SK Poliomyelitis Virus, *Arch. Biochem.* **3**:299-303 (Feb.) 1944.

293. Toomey, J. A.: Observations on Treatment of Infantile Paralysis in Acute Stage (Nathan Lewis Hatfield Lecture), *Tr. & Stud., Coll. Physicians, Philadelphia* **12**:14-25 (April) 1944.

294. Ward, R.: The Epidemiology of Poliomyelitis, *J. Bone & Joint Surg.* **26**:829-832 (Oct.) 1944.

284. Nickle, M., and Kabat, H.: Specificity in Effects on Brain Metabolism of Two Differing Neurotropic Viruses, *J. Exper. Med.* **80**:247-255 (Sept.) 1944.

285. Gellhorn, E.: Effect of Muscle Pain on Central Nervous System at Spinal and Cortical Levels, *Journal-Lancet* **64**:242-245 (July) 1944.

286. Kabat, H.; Erickson, D.; Eklund, C., and Nickle, M.: Decrease in Lactic Acid Content of Brain in Poliomyelitis, *Science* **98**:589-591 (Dec. 31) 1943.

287. Carey, E. J.: Study on Ameboid Motion and Secretion of Motor End-Plates: Anatomic Effects of Poliomyelitis of Neuromuscular Mechanism in Monkey, *Am. J. Path.* **20**:961-995 (Sept.) 1944.

288. Gard, S.: Observations Concerning the Pathogenesis and the Epidemiology of Mouse Poliomyelitis, *Yale J. Biol. & Med.* **16**:467-476 (May) 1944.

They discuss the previous methods of treatment, including amino acids, vitamins, glandular preparations and other agents. They report extensive studies of basal metabolic rates, tolerance tests, and other aspects of the disease. Their study of the distribution shows the definite hereditary nature of the condition.

Mackay<sup>352</sup> presents an interesting case of dystrophy and the status of treatment at the present time. The particular type which he describes is the Charcot-Marie-Tooth type.

Schwartz<sup>353</sup> also describes the various effects of progressive neuropathic (peroneal) muscular atrophy (Charcot-Marie-Tooth disease), pointing out the inheritance factors as well as the clinical observations.

*Ataxia.*—Brugsch and Hauptmann<sup>354</sup> describe an interesting combination of Friedreich's ataxia in combination with neuropathic (peroneal) muscular atrophy (Charcot-Marie-Tooth disease).

*Neuralgia.*—Doupe, Cullen and Chance<sup>355</sup> discuss the causal type of pain that is found in post-traumatic neuralgia.

*Diagnostic Procedures.*—There has been considerable work done in electromyographic study on the various forms of nerve-muscle disturbances in the last few years.

Brazier, Watkins and Schwab<sup>356</sup> illustrate the difference in various types of polyneuritis and poliomyelitis with regard to electromyographic records.

Hoefer and Guttman<sup>357</sup> have made extensive electromyographic studies to determine the level of spinal cord lesions. They present the results in 24 cases and conclude that motor unit discharges recorded from the relaxed muscles may indicate the level of a lesion of the spinal cord, even in the absence of clinical manifestations suggestive of involvement of the anterior horn

cells or motor roots. In 17 of 24 cases the lesion was satisfactorily localized, and in the others fairly close localization was obtained; false localization was obtained in only 2 cases.

De Jong<sup>358</sup> has devised an instrument for electrical examination and treatment of peripheral nerves, which is a small light unit and accomplishes many purposes by virtue of features usually not combined in a single instrument.

Pollock and others<sup>359</sup> have studied denervated muscles with various amperages of current and noted the changes which occur when regeneration is taking place.

Licht<sup>360</sup> has formulated an outline of electrodiagnosis of neuromuscular disease for the army.

*Surgery.*—Cerebral Palsy: Chandler<sup>361</sup> described the surgical procedures which are in present use for correcting deformities of spastic paralysis and the indications for and the various results obtained by the different operations.

Peripheral Nerve: Schulze<sup>362</sup> has described a method of operation for correcting the deformities due to paralysis of the trapezius muscle.

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362. Schulze, R.: Trapezius Paralysis: Surgical Therapy, Zentralbl. f. Chir. 70:692 (May 8) 1943.

363. Huguier, J., and Nardi: Complete Impotence of Arm Due to Traumatic Elongation of Brachial Plexus: Arthrodesis of Shoulder and of Wrist with Tendon Transplants; Satisfactory Functional Result, Mém. Acad. de chir. 68:168-173 (Feb. 11-March 4) 1942.

364. Weiss, P.: Sutureless Reunion of Severed Nerves with Elastic Cuffs of Tantalum, J. Neurosurg. 1:219-225 (May) 1944; Technology of Regeneration: Review; Sutureless Tubulation and Related Methods of Nerve Repair, ibid. 1:400-450 (Nov.) 1944.

352. Mackay, R. P.: Progressive Muscular Dystrophy. Proc. Interst. Postgrad. M. A. North America (1943), 1944, pp. 88-91.

353. Schwartz, L. A.: Clinical, Histopathologic and Inheritance Factors in Peroneal Muscular Atrophy (Charcot-Marie-Tooth Type), J. Michigan M. Soc. 43: 219-230 (March) 1944.

354. Brugsch, H. G., and Hauptmann, A.: Familial Occurrence of Friedreich's Ataxia with Charcot-Marie-Tooth Neural Muscular Atrophy, Bull. New England M. Center 6:42-48 (Feb.) 1944.

355. Doupe, J.; Cullen, C. H., and Chance, G. Q.: Post-Traumatic Pain and Causal Syndrome, J. Neurol., Neurosurg. & Psychiat. 7:33-48 (Jan.-April) 1944.

356. Brazier, M. A. B.; Watkins, A. L., and Schwab, R. S.: Electromyographic Studies of Muscle Dysfunction in Infectious Polyneuritis and Poliomyelitis, New England J. Med. 230:185-189 (Feb. 17) 1944.

357. Hoefer, P. F. A., and Guttman, S. A.: Electromyography as Method for Determination of Level of Lesions in Spinal Cord, Arch. Neurol. & Psychiat. 51: 415-422 (May) 1944.

and Kenny technic. Of the 21 cases, there were good to excellent end results in all. The modification of the Kenny technic consisted in the elimination of hot packs and the substitution of prostigmine, usually orally but occasionally parenterally as well. No change was made in the usual methods of muscle reeducation of or in the passive joint movement procedure. He states, "Approximately 75 per cent of patients with poliomyelitis can be adequately cared for at home without special nursing attention with this technique." Boines also urges the extension of this method of therapy especially in chronic cases.

McFarland and colleagues<sup>312</sup> make a preliminary report of a series of 74 selected cases in which neurotripty was combined with the Kenny treatment. In 25 of these cases neurotripty was given while the Kenny treatment was being given in the acute stage, and in 49 cases of longstanding residual paresis neurotripty also was given in combination with the Kenny method. The rationale of neurotripty is the fact that in regrowth after nerve interruption there is an increased branching. The authors present an outline of the procedure, which is done with general or spinal anesthesia with the objective of breaking as many branches of the remaining five motor nerve axons as possible. The technic is to knead through the muscle vigorously and deeply with a blunt instrument. The muscle is covered thoroughly throughout its entire extent. There has been a rather consistent increase in circulation in the involved segments, and an increase in muscle size is a "frequent result." Improvement in muscle strength occurred in over one half of one hundred and thirty muscle groups studied. "The results are encouraging."

Miley<sup>313</sup> presents a preliminary report on 38 cases in which the Knott technic of ultraviolet irradiation of blood was used in addition to the Kenny treatment. There were no harmful effects in this series of cases. This technic did not interfere with the Kenny routines. No attempt was made to evaluate the ultimate end results for these patients, but it is Miley's conclusion that further extensive clinical studies with this combination of treatments is warranted.

Nelson<sup>314</sup> discusses the present status of poliomyelitis. Regarding treatment, he says that hot

packs during the stage of spasm followed by muscle reeducation offer the most help in the acute stages.

Compere<sup>315</sup> outlines the management and care of patients with infantile paralysis. He states that his own observation led to the conclusion that the earlier the program of treatment of peripheral manifestations is done the better are the end results. Microscopic sections of muscles that are in spasm show a picture of pathologic congestion. This congestion may be relieved by hot packs, passive motion and active exercise. He further concludes that the number of patients who will require surgical intervention may be as large as that of the patients who have received other types of treatment but that the patients given treatment by hot packing, early activity, exercises and good physical therapy will be in better condition generally and will thus obtain greater profit from the efforts of the orthopedic surgeon.

Wright<sup>316</sup> presents problems encountered in the early treatment of poliomyelitis. She states that Kenny has made a valuable contribution but that one will continue to use to advantage the Silver method of the prevention of stasis of the circulation by special postural measures in bed, the Lovett-Merrill method of muscle testing, the Kendall percentage grading, the Lowman under water reeducation and the light, efficient supports when indicated. In a second article, Wright<sup>317</sup> outlines a reasonable program of treatment for acute poliomyelitis. She notes that "treatment can not be by one method only but must meet the needs of each case."

Wolf<sup>318</sup> in discussing the clinical aspects of poliomyelitis, states that "when a patient with pure bulbar poliomyelitis is placed in a respirator it can be seen that more harm than good results. The patient breathes with the machine at times and against it at others. The use of the respirator under these conditions may be extremely harmful."

Thompson<sup>319</sup> discusses the Kenny method and correlates a program of occupational therapy combined with the Kenny method.

315. Compere, E. L.: Management and Care of the Infantile Paralysis Patient, *Arch. Phys. Therapy* **24**: 709-712 (Dec.) 1943.

316. Wright, J.: Problems in Early Treatment of Poliomyelitis, *New York State J. Med.* **44**:67-72 (Jan. 1) 1944.

317. Wright, J.: Reasonable Treatment of Acute Poliomyelitis, *Pub. Health Nursing* **36**:510-515 (Oct.) 1944.

318. Wolf, A. M.: Symposium on the Management of Poliomyelitis, *Am. J. Dis. Child.* **67**:332-334 (April) 1944.

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312. McFarland, J. W.; Billig, H. E., Jr.; Taylor, G. M., and Dail, C. W.: Kenny Treatment Combined with Neurotripty in Care of Poliomyelitis, *Arch. Phys. Therapy* **25**:645-650 (Nov.) 1944.

313. Miley, G.: Ultraviolet Blood Irradiation Therapy in Acute Poliomyelitis, *Arch. Phys. Therapy* **25**: 651-656 (Nov.) 1944.

314. Nelson, N. B.: Poliomyelitis: Its Present Status, *California & West. Med.* **60**:18-21 (Jan.) 1944.

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They discuss the previous methods of treatment, including amino acids, vitamins, glandular preparations and other agents. They report extensive studies of basal metabolic rates, tolerance tests, and other aspects of the disease. Their study of the distribution shows the definite hereditary nature of the condition.

Mackay<sup>352</sup> presents an interesting case of dystrophy and the status of treatment at the present time. The particular type which he describes is the Charcot-Marie-Tooth type.

Schwartz<sup>353</sup> also describes the various effects of progressive neuropathic (peroneal) muscular atrophy (Charcot-Marie-Tooth disease), pointing out the inheritance factors as well as the clinical observations.

*Ataxia.*—Brugsch and Hauptmann<sup>354</sup> describe an interesting combination of Friedreich's ataxia in combination with neuropathic (peroneal) muscular atrophy (Charcot-Marie-Tooth disease).

*Neuralgia.*—Doupe, Cullen and Chance<sup>355</sup> discuss the causalgic type of pain that is found in post-traumatic neuralgia.

*Diagnostic Procedures.*—There has been considerable work done in electromyographic study on the various forms of nerve-muscle disturbances in the last few years.

Brazier, Watkins and Schwab<sup>356</sup> illustrate the difference in various types of polyneuritis and poliomyelitis with regard to electromyographic records.

Hoefler and Guttman<sup>357</sup> have made extensive electromyographic studies to determine the level of spinal cord lesions. They present the results in 24 cases and conclude that motor unit discharges recorded from the relaxed muscles may indicate the level of a lesion of the spinal cord, even in the absence of clinical manifestations suggestive of involvement of the anterior horn

cells or motor roots. In 17 of 24 cases the lesion was satisfactorily localized, and in the others fairly close localization was obtained; false localization was obtained in only 2 cases.

De Jong<sup>358</sup> has devised an instrument for electrical examination and treatment of peripheral nerves, which is a small light unit and accomplishes many purposes by virtue of features usually not combined in a single instrument.

Pollock and others<sup>359</sup> have studied denervated muscles with various amperages of current and noted the changes which occur when regeneration is taking place.

Licht<sup>360</sup> has formulated an outline of electrodiagnosis of neuromuscular disease for the army.

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changed to regular plaster of paris bandages padded at pressure points with cottonoid, and just before application of the cast sulfanilamide powder was dusted over the leg and between the toes. The leg of each animal which showed the lesser maximum deviation from the normal mean was the one chosen for immobilization, and in order to be used this deviation had to be below 10 per cent. These data for 18 typical cats are summarized in table 1. With these modifications, 18 of the 22 cats withstood a six week period in the cast, 8 in the relaxed, 5 in the neutral and 5 in the stretched position. One week was allowed after removal from the cast for reestablishment of normal joint action and subsidence of edema before the initial stimulation was made. Records were obtained once a week for the first four weeks after removal of the cast and every two weeks after that for a total of eight weeks. Thirteen cats were followed for the

groups, however, shows a great individual variation both between members of the group and between individual stimulations of the same animal. Because of this variation, there is no consistent loss or gain in strength in the groups in the neutral or in the relaxed position. If the great loss of cat 77 and the gain of cat 76 are omitted, the group in the relaxed position shows little significant variation from the mean normal value. In the group in the neutral position the reason for the gain in strength of cat 84 and the pronounced loss of strength terminally of cat 54 is not apparent. On the other hand, all 5 of the animals in the stretched position showed significant loss in the first week and remained

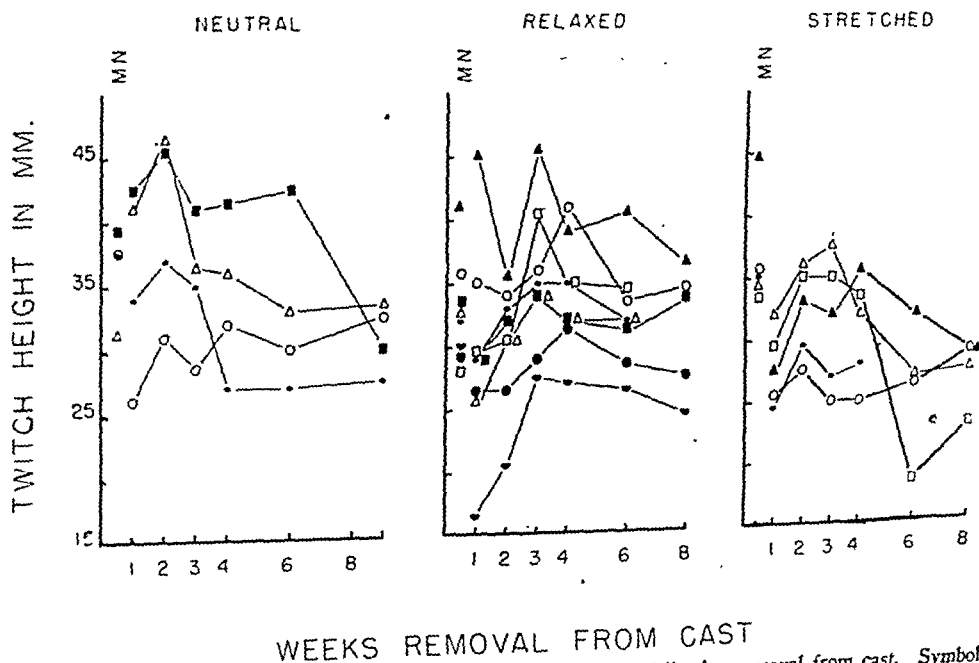


Fig. 4.—Graph showing twitch height in disuse atrophy of muscles following removal from cast. Symbols in column under *MN* represent mean normal twitch height for each animal. Each symbol represents a different cat.

entire eight week period and 3 cats for six weeks. Data appear in table 2 and are represented graphically in figure 4.

The significant variation from the mean normal twitch strength is summarized in table 3. This is taken as that variation from the mean normal twitch strength which is in excess of the maximum deviation from the mean normal and is calculated as per cent of mean normal twitch strength. Taking the average for the groups, these data show that one week after removal of the cast the neutral legs showed no loss of strength while the relaxed legs had lost approximately 10 per cent and the stretched legs 20 per cent and that the stretched group remained consistently below the mean normal value. Analysis of the data for each cat in all the

below the mean normal value for the whole period of stimulation, whereas, of the 5 animals in the other groups showing significant loss of strength in the first week, 3 had returned to approximately normal by the end of the second week and 4 by the end of the third week. These data then indicate that six weeks' immobilization of normal muscles in the stretched position brings about moderate and persistent disuse atrophy, whereas immobilization in the neutral and in the relaxed position has little consistent effect, and that the relaxed position is no more conducive to disuse atrophy than is the neutral position.

It is to be noted that in this group the first tests were done one week after the casts were

removed. This gave time for the muscle to regain its tone, for its circulation to return to an approximately normal condition and for the joints to limber up. We recognize the fact that there was some recovery of power in the muscles during this week but believe that the tests made immediately after the removal of the immobilization are apt to give false impressions, and this is especially true of a muscle which has been immobilized in a position of relaxation.

Further analysis of the data presents several difficulties. The degree of variation of strength from one stimulation to the next in the same animal is unexplained. It is difficult to believe that it is due to a technical error on the part of the operator, since the same technic of stimulation was observed after immobilization as before. The average maximum variation from the mean in at least three stimulations before

sectioning the sciatic nerve at the level of the ischial tuberosity and suturing the two ends back under the muscle so that they were directed away from each other. At the conclusion of the experiment when the gastrocnemius muscles were dissected free and weighed, the area of nerve section was carefully inspected and no evidence of union found in any of the animals, the ends of the nerve being in most cases  $\frac{1}{2}$  to  $\frac{3}{4}$  inch (1.2 to 1.9 cm.) apart.

Twelve of these animals were denervated and not immobilized. These controls were stimulated once a week in order to determine the normal course of atrophy measured by our apparatus. Nine of the animals were followed for six weeks or more and 6 of them for as long as ten weeks. The other 12 animals were denervated and immobilized immediately for a period of six weeks, 6 in the stretched and 6 in the relaxed position. Another 6 would have been immobilized in the neutral position, but the control group had shown our method to be unreliable for stimulation of denervated muscle.

Denervation of muscle increases the time-strength characteristic (chronaxia), as shown by

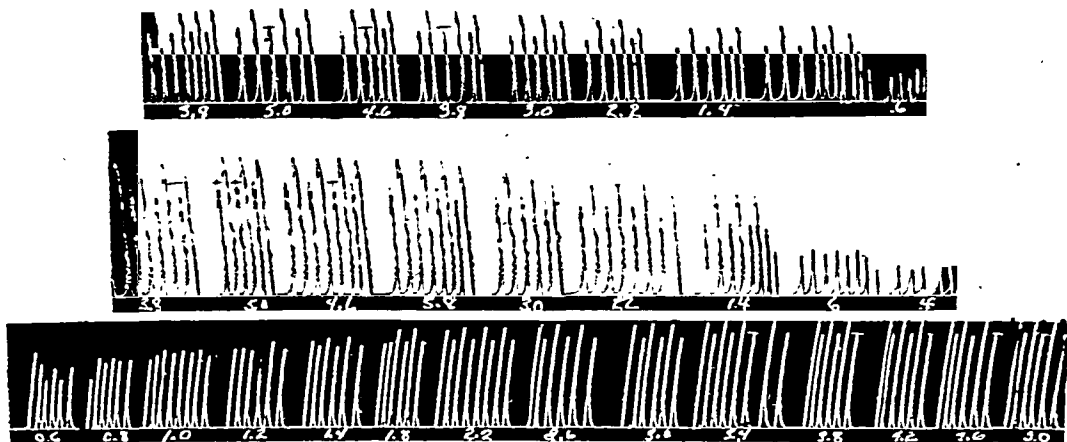


Fig. 5.—Record of twitch height in denervated muscles. Upper and middle records show no plateau. Lower record shows plateau from 3.4 to 5 amperes. Plateau height denoted by compass marks. Stimulation amperages listed below each group.

immobilization was only 4 per cent in this group and, as stated before, in a total of 51 cats not more than 4.6 per cent. Furthermore, it is peculiar that in 3 cats the muscles showed an increase in strength following immobilization.

#### OBSERVATIONS ON DENERVATED MUSCLES

The studies on denervation were carried out with the idea of determining whether immobilization had any effect in delaying or lessening the atrophy of denervation and, if so, which position was the most effective.

In 24 cats the mean normal twitch in the strength of muscles was determined by at least three stimulations one week apart, and for an animal to be used the maximum deviation from the mean had to be less than 10 per cent. The leg which showed the least deviation from the mean was chosen for denervation. This was carried out by

Adrian<sup>11</sup> (1916). Therefore the denervated legs were stimulated with only 20,000 and 30,000 ohms in the secondary, thus producing a longer-acting stimulus. Still no definite plateau could be obtained consistently. Sometimes a plateau from 3.8 to 5 amperes could be recorded, while at other times no plateau could be found even up to 5 amperes (fig. 5). This applied to stimulation of an individual muscle from week to week as well as to the group as a whole. We attributed this inability to obtain a plateau in the denervated muscles to several factors. With denervated muscle, excitation is entirely through the muscle fibers and, in contrast to the disuse atrophy muscles, no nerve stimulation occurs.

11. Adrian, E. D.: The Electrical Reaction of Muscles Before and After Nerve Injury, *Brain* 39:1-33, 1916.

The muscle itself requires a longer period of stimulation before reacting to the current, as mentioned before. The mass of muscle was so great and the spread of the exciting current so nonuniform that high current strengths were necessary before all the muscle fibers could be reached. When these current strengths were used, they were so great that the fibers closest to the electrodes were being overstimulated and, in fact, responded more than once to each shock. Shortening the duration of shock sufficiently to prevent this required unmanageable amperages that caused arcing at the switch.

that the loss in wet weight of a denervated muscle is not a reliable criterion for judging its loss in power.

#### COMMENT

We believe that the method of recording and determining the strength of a single contraction (twitch) in the gastrocnemius-soleus group of muscles at the break plateau level is a satisfactory method of determining the power of this muscle at intervals in the living animal. By this method it is possible to establish a normal for a given muscle and then to determine the strength of a single twitch of the same muscle after it has been immobilized.

Our experiments on disuse atrophy were not very satisfactory because of difficulty in maintaining the animals in good condition and in maintaining satisfactory immobilization over the desired period of six to eight weeks. (As a matter of fact, we used over 90 animals in these experiments and only results for the last groups are recorded.) From our data it seems that immobilization of an extremity over a reasonable period is not greatly detrimental to normal muscles unless they are immobilized in a stretched position. It is further to be noted that these muscles quickly recover their normal power spontaneously when set free and permitted to function, and no physical therapy is necessary. Admittedly, our immobilization was not absolute, but neither is that used clinically in plaster casts or splints.

Of the three positions used, the relaxed and neutral positions were less harmful and the stretched position was more harmful, and this conforms with our clinical observations in the past.

We realize the inadequacy of our experiments on denervated muscles and the danger of drawing conclusions from inadequate data, but it is our impression that prolonged immobilization in any position is more harmful to denervated muscles than to normal muscles. We believe that the danger of "stretch paralysis" in extremities which are not immobilized has been over-emphasized and that the paralyzed muscle is better left unsplinted, unless splints are necessary to relieve pain, to prevent deformity or to aid function in permanently paralyzed extremities.

In line with this reasoning is the question of priority in fractures of the extremities complicated by peripheral nerve lesions. We believe that when possible the nerve should be repaired without waiting for the fracture to heal or even for the infection in the bone to heal or be eradicated. With the aid of chemotherapy, this can

Realizing these limitations of the data, the plateau values or, in the many cases in which plateaus were not obtained, the highest contraction recorded with amperages up to 5 amperes were analyzed. Amperages of 3.8 or higher had to be used almost exclusively. These data show that of the control group five muscles after six weeks' denervation and four muscles after seven weeks' denervation each lost 29.4 per cent of their original strength. These nine muscles had lost an average of 21.9 per cent of their strength at the end of only one week's denervation, which would seem to indicate that not all the muscle fibers were being stimulated, or if they were it indicates an immediate loss of strength on denervation of muscle followed by a much more gradual loss. Even if not all the fibers are stimulated, the loss in strength from 21.9 per cent to 29.4 per cent in six weeks' denervation may indicate the speed of the change occurring in the muscle, because the current spread is the same and the same proportionate number of fibers would be reached with each stimulation. In the groups which were denervated and then immobilized six weeks, those muscles immobilized in the relaxed position showed an average loss in strength of 73.6 per cent in 3 cases and those immobilized in the stretched position lost approximately 51.8 per cent in 5 cases.

In the denervated animals, the loss in wet weight after seven weeks' denervation was practically the same in each of the three groups studied. By comparing the wet weight of the denervated muscle to that of the normal muscle, we found that the control group lost 63 per cent in 3 animals, the group which was so immobilized in a stretched position 61.6 per cent in 4 animals, and the group immobilized in relaxed position 55.9 per cent in 3 animals. This approximately equal loss in weight of the three groups does not correspond to their pronounced difference in loss of power and is further support for the feeling

be done with relative safety. We further believe that when practical internal fixation should be used for fractures complicated by nerve lesions in order that external fixation may be reduced to a minimum. For this, there may be a place for the dual plates recently described by one of us (J. A. K.).

During the course of the work, we have thought of several means to improve the method and to eliminate obstacles which were encountered. Since we cannot effect them at this time, we make them as suggestions to any one interested in carrying this work further.

1. In denervated muscle, a satisfactory plateau could probably be obtained on stimulation if smaller experimental animals were used. The main factor in our inability to obtain this plateau was the size of the muscle which was so great in cats that stimulation of all the muscle fibers required current strengths which stimulated the fibers nearest the electrodes more than once. The smaller the muscle mass, the less important this factor would be.

2. Arcing across the points of the hand switch was another difficulty. A thyrotron would eliminate this, give better control of stimulating currents and make possible their use at much higher values acting for a shorter time. It could also be set to deliver a standard number of stimuli at each current strength used, thus eliminating excess stimulation and any fatigue factor which that may introduce.

3. The twitch measures immediate power but gives no indication of endurance. A study of tetanic strength in disuse and denervation atrophy may yield important information. Such a study was not possible with our apparatus because the inductorium could not carry the necessary current strength. A thyrotron, however, would provide a means for constant strength tetanic stimulation at high currents.

#### SUMMARY

This study attempts to determine two things: (1) the optimum position of fixation of limbs in order to conserve muscle power and (2) the

best method of treatment of muscles paralyzed by loss of nerve supply.

A review of the literature on muscle physiology shows that in most of the studies of disuse and denervation atrophy weight has been used as a criterion of the atrophy. Functional studies have employed methods requiring the killing of the animal after one stimulation. Only one functional study has been reported in which the same animal was repeatedly stimulated, and this method was not satisfactory for our purpose.

A method was developed for recording the twitch strength of the gastrocnemius-soleus group of muscles in cats. By means of the described method, animals have been stimulated as much as twelve different times without noticeable ill effect.

In a series of 51 normal cats stimulated at weekly intervals, this method yielded normal values for one leg, which showed only 4.6 per cent average maximum deviation from the mean, with a maximum deviation range of 0 to 8.3 per cent.

This method was applied to the study of disuse atrophy. After normal values were determined legs were immobilized for six weeks, with the muscle group in stretched, relaxed and neutral positions. Stimulation for eight weeks following removal of the cast showed moderate and persistent disuse atrophy in the muscles which were stretched, whereas the relaxed and neutral groups showed little consistent effect.

Denervated cats also were immobilized in various positions, but the study was unsatisfactory because no definite contraction plateau could be obtained in response to stimulation.

On the basis of the data obtained from denervated cats, however, the suggestion is made that denervated muscles atrophy less if left alone than if immobilized. Emphasis is also placed on repairing the nerve before the bone is healed when fractures are complicated by peripheral nerve injuries.

Dr. George Bishop, Professor of Biophysics, Washington University School of Medicine, has given help, without which this method could not have been developed.

Clarence E. Rupe, M.D., has given technical assistance in some of these experiments.

# REESTABLISHMENT OF PANCREATIC SECRETION INTO THE INTESTINE AFTER DIVISION OF THE PANCREAS

## AN EXPERIMENTAL STUDY

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Since 1935 much progress has been made in the radical operative treatment of carcinoma involving the head of the pancreas and the periampullary region. In that year the publication of Whipple, Parsons and Mullins<sup>1</sup> opened an avenue of approach to a technical field which previously had been entered only at sporadic intervals. Numerous contributions to the technical details of the operation have appeared in the literature of recent years, and complete reviews of their development have been recorded.<sup>2</sup> As a result, the matter of pancreatic and periampullary carcinoma can be approached today

with a clearer conception of the operative technique and with a reasonable chance of accomplishing a surgical cure. Despite widening experience with this difficult surgical problem, however, the incidence of postoperative complications, some of which are fatal, remains high. Some of the more distressing postoperative sequelae are referable to the stump of the divided pancreas and consist of external pancreatic fistula, acute pancreatic necrosis, retention cyst and chemical, or "enzymatic," peritonitis.

The pancreatic stump has been handled, generally speaking, by one of two methods: occlusion by inverting sutures, with or without ligation of the duct of Wirsung, or some form of pancreaticoenterostomy, in which the stump is implanted into a segment of intestine. As regards the first method, digestion of the inverting sutures occurs all too frequently, with resultant leaking of pancreatic juice and the consequent development of one or more of the aforementioned complications. Concerning the second method, the question has been raised whether reimplantation of the pancreatic duct into the gastrointestinal tract is actually necessary, inasmuch as it is well established that many patients live normal, healthy lives after being deprived of the external secretions of the pancreas. On the contrary, numerous persons in whom the continuity of the pancreaticointestinal relationships has been disrupted suffer severely from disturbances of fat digestion in the form of steatorrhea and malnutrition. In their discussion of this matter, Pickrell and Blalock<sup>3</sup> concluded that whenever possible pancreatic secretions should be preserved by implantation of the duct into the bowel. Child<sup>4</sup> has stated that "the significant single fact is that it cannot be fore-

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1. Whipple, A. O.; Parsons, W. B., and Mullins, C. R.: Treatment of Carcinoma of the Ampulla of Vater, *Ann. Surg.* 102:763, 1935.

2. (a) Whipple, A. O.: Surgical Treatment of Carcinoma of the Ampullary Region and Head of the Pancreas, *Am. J. Surg.* 40:260, 1938. (b) Hunt, V. C.: Surgical Management of Carcinoma of the Ampulla of Vater and of the Periapillary Portion of the Duodenum, *Ann. Surg.* 114:570, 1941. (c) Orr, T. G.: Resection of the Duodenum and Head of the Pancreas for Carcinoma of the Ampulla, *Surg., Gynec. & Obst.* 73:240, 1941. (d) Trimble, I. R.; Parsons, J. W., and Sherman, C. P.: A One-Stage Operation for the Cure of Carcinoma of the Ampulla Vater and Head of the Pancreas, *ibid.* 73:711, 1941. (e) Whipple, A. O.: The Rationale of Radical Surgery for Cancer of the Pancreas and Ampullary Region, *Ann. Surg.* 114:612, 1941. (f) Pearse, H. E.: A Simplified Anastomosis for Resection of the Duodenum and Head of the Pancreas, *Surg., Gynec. & Obst.* 75:333, 1942. (g) Harvey, S. C., and Oughterson, A. W.: The Surgery of Carcinoma of the Pancreas and Ampullary Region, *Ann. Surg.* 115:1066, 1942. (h) Brunschwig, A.: The Surgery of Pancreatic Tumors, St. Louis, C. V. Mosby Company, 1942; (i) One-Stage Pancreaticoduodenectomy, *Surg., Gynec. & Obst.* 77:581, 1943. (j) Child, C. G., III: Carcinoma of the Duodenum: One-Stage Radical Pancreaticoduodenectomy Preserving the External Pancreatic Secretion; Case Report, *Ann. Surg.* 118:838, 1943. (k) Cattell, R. B.: Resection of the Pancreas: Discussion of Special Problems, *S. Clin. North America* 23:753, 1943; (l) Radical Pancreaticoduodenal Resection for Carcinoma of the Ampulla of Vater, *ibid.* 24:640, 1944.

3. Pickrell, K. L., and Blalock, A.: The Surgical Treatment of Carcinoma of the Common Bile Duct, *Surgery* 15:923, 1944.

4. Child, C. G., III: Pancreaticojejunostomy and Other Problems Associated with the Surgical Management of Carcinoma Involving the Head of the Pancreas, *Ann. Surg.* 119:845, 1944.

cast prior to operation to which group any given patient will ultimately belong" and, consequently, advocated maintenance of the external secretory function of the pancreas. Further support to the importance of preserving the pancreatic juice has been given recently by Whipple.<sup>5</sup>

When one has adopted the idea that some variety of pancreaticoenterostomy is desirable, the problem arises of developing a satisfactory technic. Experimentally, several methods have been applied, beginning in 1909 with the complicated procedure of Coffey.<sup>6</sup> In 1915 Sweet and Simons<sup>7</sup> described a method of implantation of the divided pancreatic stump of a dog into the small intestine, while Patrie, Pyle and Vale<sup>8</sup> in 1917 reported a similar procedure on dogs, with a satisfactory functional result. More recently, Person and Glenn<sup>9</sup> demonstrated the feasibility of implanting the pancreatic stump into the stomach by open anastomosis in dogs. Their results indicated that pancreaticogastrostomy produces a normally functioning fistula and that in such a situation atrophy of the pancreas, acute pancreatitis, peritonitis and deposition of lipids in the liver do not occur. Extending the matter of pancreaticoenterostomy further, Poth,<sup>10</sup> Child<sup>4</sup> and Cattell<sup>2k</sup> each have applied some form of the procedure in clinical practice, with satisfactory results.

An evaluation of the technics employed by the aforementioned investigators directs attention to two important factors: with the exception of Cattell's<sup>2k</sup> simple method, all procedures involve an open anastomosis, thereby causing a breach in asepsis, and most are too time consuming, even though mechanically simple. The radical operative treatment of periampullary and pancreatic carcinoma is a formidable test of the patient's endurance, and the conservation of time may be an important factor in the ultimate outcome. Inasmuch as the disposal of the pancreatic stump represents a terminal step in the

procedure, when the patient's vitality is lowest, the method of managing this technical detail should be uncomplicated and quickly performed. As regards asepsis, it is advisable to avoid, if possible, opening the intestine in the presence of the large raw surface created by duodenectomy. With the idea in mind of developing an aseptic technic which can be performed with minimal loss of time and by which the external pancreatic secretions can be preserved, the following experimental study was conducted.

#### METHOD

Twenty-two dogs were studied. Fifteen were subjected to operation under anesthesia induced by intravenous injections of pentobarbital sodium by the following technic. The duodenum was delivered into the wound along with the attached pancreas. The gland was divided at the junction of the uncinata process and the body without disturbing the relationships of the latter to the duodenum (fig. 1A), thereby leaving intact the junction of the main pancreatic duct with the ampulla of Vater. The exposed transected surface of pancreatic body was closed by interrupted invaginating sutures of fine silk after ligation of the divided duct (fig. 1A). In this manner, the long uncinata process (10 to 15 cm.) was isolated entirely from the remainder of the gland, maintaining its independent blood supply intact. No attempt was made to ligate the divided end of the uncinata duct, but it was allowed to retract into the parenchyma of the gland (fig. 1B). A loop of jejunum about 7 inches (17.7 cm.) from the ligament of Treitz was next brought into the wound. In the long axis of the antimesenteric surface of the jejunal loop, an incision was made of sufficient length to accommodate the cut surface of the uncinata stump. Particular care was taken to carry the incision down to, but not through, the mucosa, so that an opening into the lumen would not occur. The serosal edges of the incision were spread apart gently, and the stump of the divided uncinata process, with its retracted duct, was implanted into the jejunal wall and made secure by interrupted sutures of fine surgical gut (fig. 1C). The abdominal wound was closed in layers.

The remaining 7 animals were operated on by a modification of the technic of Cattell.<sup>2k</sup> The procedure was similar in detail to that described, except that the uncinata duct was isolated and dissected free from its surrounding parenchyma so as to protrude from the divided stump of the gland. A crushing ligature of fine surgical gut was tied tightly about the protruding duct. One end of the ligature was then passed as a suture through the exposed jejunal submucosa and tied firmly to the other end, thus bringing the crushed duct against the mucosa in a firm, necrotizing ligature (fig. 1D). The pancreatic stump was secured into the jejunal wall in the usual manner (fig. 1C).

All animals survived and remained in good condition. Each was fed the same diet of prepared commercial dog food containing relatively low concentrations of protein and fat. No particular effort was made to suppress pancreatic secretagogues.

Observations of the state of the pancreaticoenterostomy were made at intervals varying from seven to forty-eight days by the following technic. The abdomen of each dog was reopened, with the animal under anesthesia induced by intravenous injections of pentobarbital sodium, and the pancreaticoenterostomy exposed. The

5. Whipple, A. O., in discussion on Dragstedt, L. R.: Some Physiologic Problems in Surgery of the Pancreas, *Ann. Surg.* **118**:591, 1943.

6. Coffey, R. C.: Pancreatic-Enterostomy and Pancreatotomy: A Preliminary Report, *Ann. Surg.* **50**: 1238, 1909.

7. Sweet, J. E., and Simons, I. H.: Some Experiments on the Surgery of the Pancreas, *Ann. Surg.* **61**: 308, 1915.

8. Patrie, H. H.; Pyle, L. A., and Vale, C. F.: Recent Experimental Studies of the Pancreas, *Surg., Gynec. & Obst.* **24**:479, 1917.

9. Person, E. C., Jr., and Glenn, F.: Pancreaticogastrostomy, *Arch. Surg.* **39**:530 (Oct.) 1939.

10. Poth, E. J.: The Implantation of the Pancreatic Duct into the Gastrointestinal Tract, *Surgery* **15**:693, 1944.



jejunum adjacent to the pancreatic attachment was opened widely, exposing that portion of the mucosal surface apposed to the transected uncinate process. A concentrated, highly active preparation of secretin,<sup>11</sup> varying in amount from 10 to 20 cc. according to the size of the animal, was then injected into the vena cava.

In the instances in which a fistula had developed from the uncinate stump into the jejunum, pancreatic juice could be seen grossly dropping from the small ductular orifice in the mucosa within three to eight minutes of the injection. When fistula formation had not occurred no response to the secretin was noted. The potency of

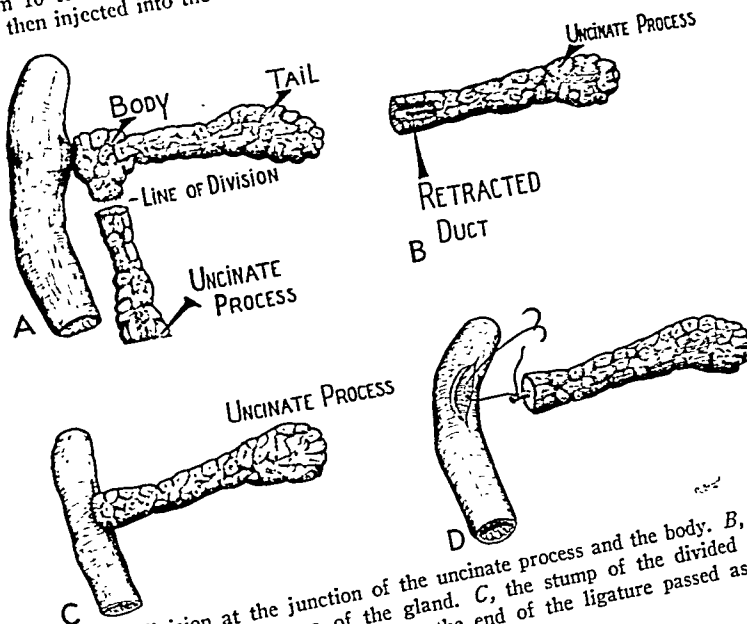


Fig. 1.—A, the line of division at the junction of the uncinate process and the body. B, the divided end of the uncinate duct retracted into the parenchyma of the gland. C, the stump of the divided uncinate process, with its retracted duct, implanted into the jejunal wall. D, the end of the ligature passed as a suture through the exposed jejunal submucosa.

*A Comparison of Findings in Experiments Performed by Us and by Cattell*

	Dog	Days Postoperatively	Gross Findings		Microscopic Changes		
			Response to Secretin	Pancreatic Stump	Acute Pancreatitis	Pancreatic Fibrosis	Pancreaticojejunal Fistula
Our technic	1	23	Positive	Soft	None	Moderate patchy	Complete
	2	23	Positive	Soft	None	Slight patchy	Complete
	3	40	Positive	Soft	Moderate diffuse	Slight patchy	Complete
	4	9	Negative	Indurated	None	Moderate diffuse	Complete
	5	7	Negative	Indurated	None	Moderate diffuse	Complete
	6	23	Positive	Indurated	Slight patchy	Moderate diffuse	Complete
	7	21	Negative	Large cyst	None	Moderate diffuse	Complete
	8	26	Negative	Soft	Large cyst	Moderate diffuse	Complete
	9	26	Positive	Soft	Slight patchy	Slight patchy	Complete
	10	21	Positive	Atrophic	None	Moderate diffuse	Complete
	11	7	Positive	Soft	None	None	Complete
	12	30	Positive	Soft	Moderate diffuse	Early slight	Complete
	13	31	Positive	Atrophic	Pronounced diffuse	Pronounced diffuse	Complete
	14	31	Positive	Indurated	None	Moderate patchy	Complete
Modified technic of Cattell	15	35	Positive	Atrophic	None	Moderate patchy	Complete
	16	48	Negative	Atrophic	None	Slight patchy	Complete
	17	7	Positive	Soft	None	Moderate diffuse	Complete
	18	29	Positive	Soft	None	Slight patchy	Complete
	19	34	Positive	Atrophic	Pronounced diffuse	Slight patchy	Complete
	20	34	Positive	Atrophic	None	Slight patchy	Complete
	21	34	Positive	Atrophic	None	Slight patchy	Complete
	22	34	Positive	Atrophic	None	Slight patchy	Complete

\* Animal died of air embolism before response could be determined.

11. Luckhardt, A. B.; Barlow, O. W., and Weaver, M.: Note on a Rapid Method of Preparing a Highly Active Pancreatic Secretin Solution, *Am. J. Physiol.* 76:182, 1926. Ivy, A. C.; Kloster, G.; Lueth, H. C., and Drewyer, G. E.: On the Preparation of Cholecystokinin, *ibid.* 91:336, 1929. Ivy, A. C.; Kloster, G.; Drewyer, G. E., and Lueth, H. C.: The Preparation of a Secretin Concentrate, *ibid.* 95:35, 1930.

the secretin was determined by opening the duodenum and observing simultaneously the increased flow of both bile and pancreatic juice from the ampulla of Vater.

After the functional status of the pancreaticojejunal junction had been determined, the entire uncinate process and several inches of the attached jejunum were excised for microscopic study of the tissues, with particular reference to acute pancreatitis, pancreatic fibrosis and development of pancreaticojejunal fistulae.

## RESULTS

None of the animals showed gross evidence of active peritonitis or fat necrosis, although local adhesions about the pancreaticoenterostomy were pronounced in 4 (18 per cent) and moderate in 11 (50 per cent); in the remaining 7 (32 per cent), adhesions were slight or absent. Other significant observations are summarized in the table.

*Response to Secretin.*—Of the 22 animals studied, 15 showed definite secretion of pan-

Among the 6 remaining failures, dogs 4, 5 and 12 were tested within nine days of the operation. Despite the negative response of dogs 4 and 5, microscopic sections showed that a junction had been made between the pancreatic duct and the jejunal mucosa, while dog 12 showed acute pancreatitis and no evidence of fistula. Two other negative responses occurred, in dogs 7 and 8, investigated at twenty-one and twenty-six days respectively. Microscopic sections in these animals revealed diffuse fibrosis of the pancreatic

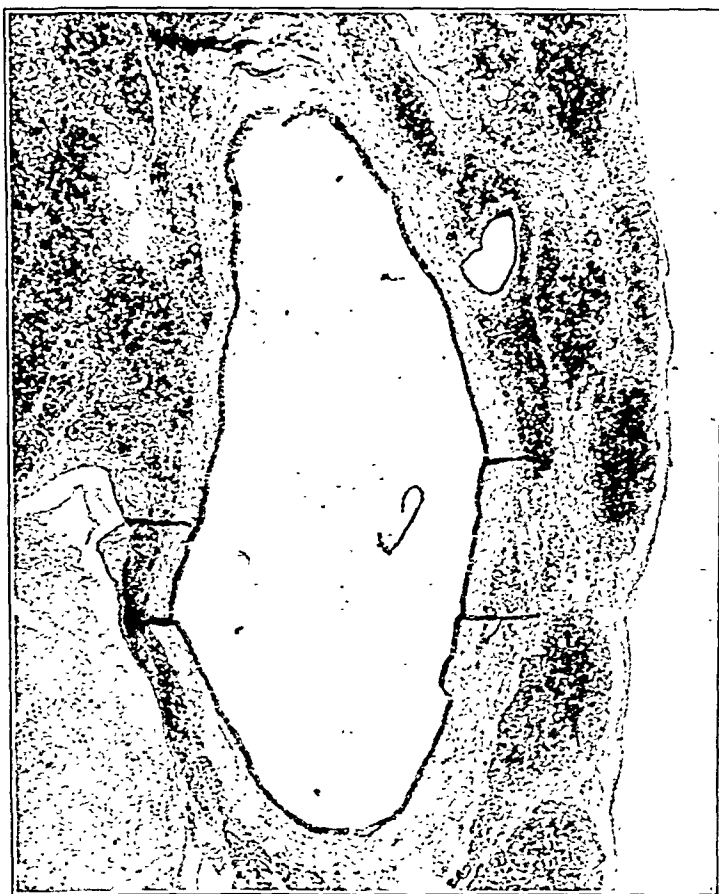


Fig. 2.—Pronounced dilatation of the duct due to obstruction from fibrosis. Note the flattened epithelial lining and the moderate degree of parenchymal scarring ( $\times 40$ ).

creatic juice at the pancreaticojejunal junction after intravenous injection of secretin, an incidence of spontaneous fistula formation of 68 per cent. One (dog 11) died of air embolism immediately after the injection of secretin into the vena cava, so that no determination of the secretory response could be made. Elimination of this animal from the series would result in an incidence of 71 per cent of spontaneous fistula formation.

stump, failure of the duct to form a junction with the jejunal mucosa and pronounced dilatation of the duct system (fig. 2). In the last failure, dog 9, a large retention cyst of the implanted stump developed, containing fluid which gave a strongly positive reaction for amylase.

*Acute Pancreatitis.*—Microscopic studies of the implanted pancreatic stumps revealed some evidence of acute inflammatory reaction in 6 animals; an incidence of 27 per cent. As noted in the table, pronounced diffuse pancreatitis was

and 19. The small duct was dissected free from the pancreatic parenchyma in the distal portion of the uncinata process. Injection of water into the duct through a hypodermic needle resulted in appearance of the water in the jejunal lumen at the fistulous opening.

#### COMMENT

An evaluation of the results of this study should pertain primarily to the functional effectiveness of the pancreaticojejunostomy as re-

This study was designed to develop not only an aseptic and time-saving method of disposal of the pancreatic stump but also a means of preserving the external secretion of the pancreas. Regarding the latter phase of the problem, results have been satisfactory, although some frank failures have occurred. Seven animals showed absence of secretory activity at the pancreatocenterostomy after intravenous injection of secretin. One of these, dog 11, died of air embolism (see preceding section) and can be ex-

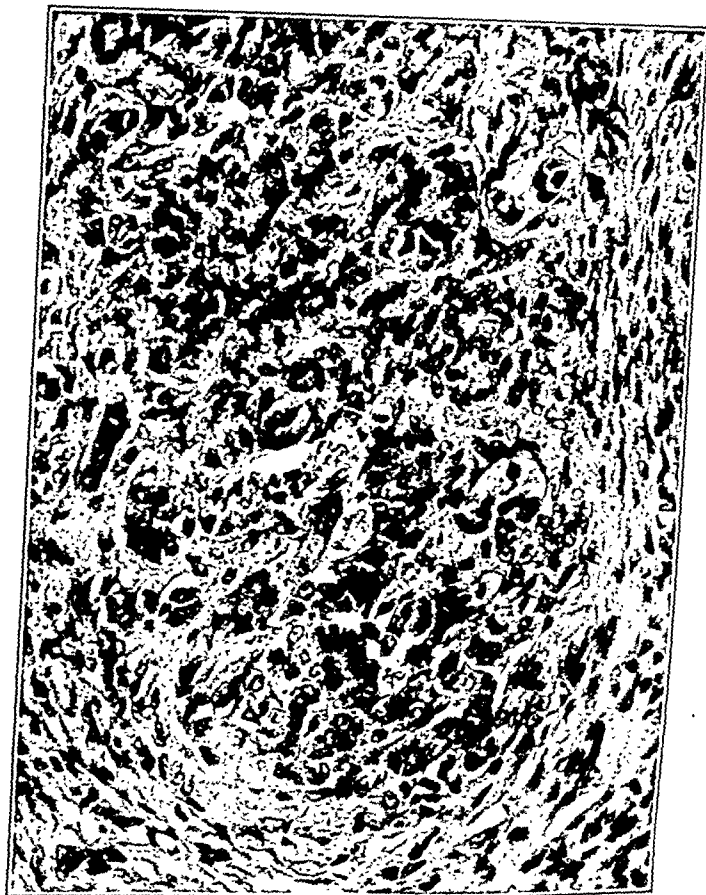


Fig. 5.—High power field of figure 4. Note the limited preservation of normal acinar elements.

gards the usual complications of radical pancreatic surgical treatment. The latter sequelae consist of external pancreatic fistula, acute pancreatitis, retention cyst and chemical peritonitis. The incidence of severe acute pancreatitis was 9 per cent in the animals studied, while only one retention cyst was found. There was no external pancreatic fistula and no peritonitis. On the basis of these results, it can be concluded that aseptic pancreaticojejunostomy in dogs according to the technic outlined is attended by a low incidence of the complications which commonly follow division of the pancreas.

cluded from the series. Of the remaining 6, dogs 4, 5 and 12 were studied nine, seven and seven days, respectively, after operation. There was neither pancreatitis nor fibrosis of notable extent of the implanted stump in dogs 4 and 5, while each was found to have microscopic evidence of a junction between the duct epithelium and the jejunal mucosa. Inasmuch as there was demonstrated none of the factors which may interfere with secretion, the question arises as to how early secretory activity may begin after pancreatocenterostomy. Dog 12, although apparently healthy, showed microscopic evidence

of pronounced diffuse acute pancreatitis unaccompanied by fat necrosis. This factor, in association with the short postoperative interval, was considered sufficient explanation for failure of secretion to occur. The other failures were dogs 7, 8 and 9, all killed three weeks or more after operation. The first 2 showed moderate diffuse fibrosis with considerable dilatation of the duct (fig. 2), and no evidence of pancreatitis, indicating that obstruction of the duct resulted from fibrosis of the adjacent parenchyma. In dog 9 a large retention cyst developed which replaced the entire uncinate parenchyma, owing to failure of the duct to break through the jejunal wall. Studies of the excised specimens of dogs 7, 8 and 9 failed to reveal any explanation of the selective action of fibrous tissue in causing obstruction of the ducts. Furthermore, it could not be determined from the investigations what factors decided whether cyst formation or simple dilatation would occur.

Varying degrees of acute pancreatitis occurred in 6 animals. Two of these showed evidence of slight patchy inflammation, principally around the sutures; 2, moderate diffuse reactions which did not interfere with secretion and 2, extreme diffuse inflammatory infiltration. In those animals in which the uncinate duct was allowed to retract into the parenchyma of the gland, a collection of pancreatic juice might be expected to develop at the site of implantation, pending spontaneous breakthrough into the jejunum, in a high percentage of instances. In such circumstances, diffuse pancreatic necrosis would be inevitable in a considerable number of cases. The development of slight, patchy, acute pancreatitis in 2 dogs and moderate diffuse pancreatitis in 2 is evidence that such a situation does not occur frequently. On the other hand, a crushing ligature about the duct, holding it firmly against the jejunal submucosa, should minimize the local accumulation of pancreatic secretion and thereby eliminate the subsequent development of diffuse pancreatitis. Actually, the only 2 instances of severe pancreatitis occurred in animals subjected to the latter technic. The first was found in dog 12, investigated seven days after operation and showing a negative response to secretin. The second was found in dog 21, thirty-four days postoperatively, in which the reaction to secretin was positive. In the latter animal, the pancreatitis was acute and the fibrosis was minimal, indicating that the inflammatory process developed late in the postoperative course. The interesting aspects of this case pertain to the pathogenesis of the pancreatitis and to the possibilities of its late effects had the animal been allowed to live longer. At the

time the dog was killed, there was no obvious condition to suggest a disease of any kind.

Despite the fact that 15 dogs presented no evidence of acute pancreatitis, some degree of fibrosis was noted in all but 2 of the total number. This situation may be interpreted as meaning that at some period of the postoperative course inflammatory infiltration of the implanted stump occurred, being displaced by scar tissue at a later date. If this reasoning is correct, it is suggested that acute pancreatitis develops shortly after operation in the majority of animals, is limited in its scope and is successfully replaced by fibrous tissue proliferation. An important observation is the fact that of 18 animals showing varying degrees of fibrosis of the stump (omitting dogs 5, 9, 11 and 20; see the table), only 4 showed a negative response to secretin. It is significant that considerable amounts of acinar tissue can be replaced by scar without eliminating the secretory function of the gland (fig. 4). Apparently, as noted in dogs 7, 8 and 9 (see the preceding section), scarification interferes with function only when it causes obstruction of the duct. There are no possible means of predicting this selective action before pancreaticojejunostomy is performed, but its incidence is low in the animals studied in this series.

#### SUMMARY AND CONCLUSIONS

An aseptic technic of implanting the transected uncinate process of the dog's pancreas into the wall of the jejunum is described.

Spontaneous fistula formation developed between the divided pancreatic stump and the jejunum in 71 per cent of the animals, as determined by the appearance of pancreatic juice at the fistula after intravenous injection of secretin.

A low incidence of the usual complications of transection of the pancreas occurred, there being no peritonitis, no external pancreatic fistula, 1 retention cyst and 2 instances of severe acute pancreatitis.

All animals survived and remained in good health regardless of whether complicating factors developed or whether pancreaticojejunal fistulas were formed.

A significant fact noted was that fibrous tissue infiltration of the implanted pancreatic stump can occur to a considerable extent without interfering with the secretory function of the gland.

Results obtained in this study suggest application of the methods described to patients undergoing radical surgical treatment of carcinoma involving the head of the pancreas and the periampullary region, for whom preservation of the external secretion of the pancreas is desired.

# INTUSSUSCEPTION OF THE VERMIFORM APPENDIX

REPORT OF A CASE

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Intussusception of the appendix into itself is rare, and only 2 cases have previously been reported. The purpose of this paper is to report another case and to discuss the pathologic picture and possible etiologic factors of this condition.

Frazer (1943)<sup>1</sup> stated that at the time of his report there had been about 100 cases of appendicular intussusception of all types recorded in the literature. He added 7 more and reviewed 75 out of the 100 previously reported. This group included all three types of intussusception: (a) simple, i. e., into itself; (b) the appendix invaginating into the cecum, either partial or complete, and (c) compound, i. e., the appendix invaginating into the cecum and the cecum into the ascending colon. This paper deals with the simple type of intussusception and adds a third case of this kind.

F. Whitrow (1930)<sup>2</sup> presented the first case report. Her patient was a 12 year old boy who was admitted to the hospital with a history typical of acute appendicitis of eighteen hours' duration. At operation the appendix was found to be the site of intussusception, the tip having invaginated itself until it lay at the base of the appendix. An appendectomy was performed, and the patient's recovery was uneventful.

The second case was reported by Frazer in 1943. His patient was a 75 year old woman who had both intussusception of the appendix and carcinoma of the cecum. In this instance, the appendicular intussusception was at the base of the appendix, where the walls were telescoped on themselves for  $\frac{1}{2}$  inch (1.3 cm.). The patient's symptoms were referable to the cancer of the large bowel, and the intussusception was observed incidentally.

All other cases of appendicular intussusception which have been reported are of the compound type. The earliest case was described in the *Edinburgh Medical Journal* in 1859 by McKidd.<sup>3</sup> The patient was a 7 year old boy who had severe

abdominal pain for two months prior to death. At autopsy the appendix was found to be intussuscepted into the cecum, which, in turn, was intussuscepted into the ascending colon. McGraw<sup>4</sup> in 1897 reported the first successful operative case. He found an intussusception of the compound variety and was able to resect the invaginated cecum and appendix without difficulty.

The causation of appendicular intussusception has been explained as follows: The appendix is capable of rhythmic peristaltic contraction; these contractions on encountering an area of inflammation within the wall of the appendix or an adherent concretion result in a buckling inward of the mucosa followed by the muscularis and serosa, with the development of an intussusception. If the base of the appendix is constricted and a foreign body or fecalith becomes impacted, the forceful peristaltic action of the appendix may carry that organ into the cecum. Previous inflammatory processes, such as acute appendicitis, may therefore set the stage for intussusception. Intussusception of the tip of the appendix is more difficult to explain because the leading point is small. There should be some nodule at the tip in these rare cases to serve as the starting point. In our case there was definite microscopic endometriosis in the ovaries, and clinically it was present in the gross specimen of the appendix. Owing to the loss of the appendix before it was sectioned, the endometriosis in that organ was not proved.

The history given by a patient with appendicular intussusception is usually that of crampy pain in the center of the abdomen, with tenderness in the right iliac fossa. Colic is characteristic and is severe; vomiting may occur, and some patients pass blood by rectum. On physical examination the patient has signs of inflammation in the right lower abdominal quadrant, and occasionally a mass is palpable above McBurney's point. In the more complicated cases, barium sulfate enema has in some instances demonstrated the intussusception of the cecum.

4. McGraw, T. A.: *Brit. M. J.* 2:956, 1897.

1. Frazer, K.: *Brit. J. Surg.* 31:23, 1943.

2. Whitrow, F.: *Brit. M. J.* 2:181, 1930.

3. McKidd, J.: *Edinburgh M. J.* 4:793, 1859.

into the ascending colon. If the intussusception becomes compound, then the clinical picture is that of intestinal obstruction.

The treatment of intussusception of the appendix into itself is appendectomy. In the event of a completely intussuscepted appendix, the appendix is removed by resecting a small cuff of cecum which surrounds the base of the appendix. The compound variety may be easily reduced, but if gangrenous, resection of a portion of the cecum and anastomosis of the ileum to the ascending or transverse colon are required.

#### REPORT OF A CASE

A 45 year old bipara was seen by a physician three years prior to operation for severe pain of twelve hours' duration in the right lower quadrant. The sudden acute pain was associated with nausea, vomiting and abdominal tenderness. Physical examination demonstrated tenderness without spasm in the right lower quadrant, a normal uterus and normal vaults. Her white blood cell count was 22,500, blood pressure 96 systolic and 60 diastolic and pulse rate 64. The urine was normal. Her pain and tenderness subsided in forty-eight hours, and she was well until one month later, when a similar pain in the right lower quadrant of the abdomen occurred. During the next six months she was free of pain, and physical examination revealed no abnormalities on three occasions. Two years later the pain recurred, associated with a slight fever. Still later the patient was referred to us. We found nothing abnormal on abdominal examination but an enlarged uterus. There was a large cystic mass in the right vault. On Nov. 24, 1943, with the patient under nitrous oxide, oxygen and ether anesthesia, an appendectomy, total hysterectomy and bilateral salpingo-oophorectomy were performed. The appendix was short and broad, and the junction of the appendix and cecum was unusually wide, measuring 1.5 cm. Because of its wide base, the appendix was removed between two Kocher clamps and the stump closed with two rows of chromic surgical gut stitches. Both ovaries were destroyed by large endometriomas which were adherent to a uterus containing fibroids and also to the under surfaces of the broad ligaments. The patient made an uneventful recovery.

*The Specimen.*—The distal half of the appendix had intussuscepted into the proximal half, and the invaginated mucosal surface of the tip of the appendix was smooth and glistening and was not ulcerated. The inverted end filled the wide lumen of the appendix, and the tip lay almost at the junction of the appendix and the cecum. In the accompanying drawing the wide base of the appendix is illustrated, as is the relationship between



Showing the wide base of the appendix and the relationship between appendix and cecum. At lower right the slight dimple at the end of the appendix is shown.

the cecum and the appendix. An end on view of the appendix is shown to demonstrate the slight dimple present, and on either side of the dimple there were bluish spots which were undoubtedly small endometriomas. Because of the loss of the appendix before microscopic examination, the diagnosis of endometriosis cannot be substantiated.

The first attack of pain, three years before operation, was undoubtedly acute appendicitis. This inflammatory process may well account for the subsequent development of the intussusception. The recurrence of the pain which necessitated further examination and operation in all probability was due to the intussusception, although the large endometriomas may have played some part in the production of the abdominal pain.

# PROGRESS IN ORTHOPEDIC SURGERY FOR 1944

## A REVIEW PREPARED BY AN EDITORIAL BOARD OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

I. DISEASES OF GROWING AND OF ADULT BONE  
PREPARED BY JOHN A. SIEGLING, M.D., CHARLESTON, S. C.

**Caisson Disease.**—Since the report of Kahlstrom, Burton and Phemister in 1939, considerable interest has been manifested in aseptic necrosis of bone as a result of caisson disease. It was predicted by Hertzmark<sup>1</sup> in 1942 that the incidence of bone changes similar to those in caisson disease would increase with the widespread use of the submarine and the high altitude flying in modern warfare. This is not borne out, however, for a review of the past year's literature reveals a dearth of material on the subject. Taylor,<sup>2</sup> in two articles covering essentially the same material, presents observations in 12 cases of occupational exposure and 38 of patients who had never worked under compressed air. The articles are interesting in that he reports cases of aseptic necrosis of caisson disease in persons not exposed to increased atmospheric compression. No theory as to the causation of the lesion in persons not working in caissons is advanced.

**Osteitis Deformans.**—Reifenstein and Albright<sup>3</sup> give an excellent presentation of a new concept of osteitis deformans (Paget's disease). Normal bone metabolism, metabolic abnormalities in osteoporosis as opposed to those in osteomalacia and osteitis fibrosa generalisata and the morbid anatomy of Paget's disease are reviewed with clarity. Two case reports are presented in which it is made clear that immobilization of fractures leads to a pronounced increase in urinary calcium and even hypercalcemia, which may be sufficient to bring about chemical death.

1. Hertzmark, M. H.: Bone Changes in Caisson Disease: Report of a Case, *Bull. Hosp. Joint Dis.* **3**: 128-133 (Oct.) 1942.  
2. Taylor, H. K.: Aseptic Necrosis and Bone Infarcts in Caisson and Non-Caisson Workers, *New York State J. Med.* **43**: 2390-2398 (Dec. 15) 1943; Aseptic Necrosis in Adults: Caisson Workers and Others, *Radiology* **42**: 550-569 (June) 1944.

3. Reifenstein, E. C., Jr., and Albright, F.: Paget's Disease: Its Pathologic Physiology and the Importance of This in the Complications Arising from Fracture and Immobilization, *New England J. Med.* **231**: 343-355 (Sept. 7) 1944.

Warning signs of hypercalcemia are listed as nausea and emesis. A hitherto undescribed sign to which attention is called, is a sensation of dryness in the throat with dysphagia. In cases in which hypercalcemia and hypercalciuria develop, the authors make it clear that treatment is simple and consists of low calcium diet and fluids given intravenously to keep the serum and urinary calcium levels low. A minimum of immobilization is advisable. The authors' interpretation of the pathologic physiology of Paget's disease is as follows and is rational: The initial lesion is destructive and has no respect for structural requirements. Destruction renders the involved bone more susceptible to stresses and strains. As a compensatory factor, the osteoblasts are stimulated to lay down more matrix; the serum phosphatase level therefore rises. In bones in which stresses and strains are always present, repair occurs concomitantly with destruction; in bones in which stresses and strains are minimal, as in the skull, repair may lag behind destruction. The joints between new and old bone are marked by cement lines, of which there are many, and since the local destructive factor has no respect for the mechanical requirements of the skeleton, the lines have no order and therefore are mosaic in character. A bone of poor architectural value results, explaining three of the striking clinical characteristics of the disease: the pronounced tendency to overgrowth of bone, the high level of serum phosphatase per unit of diseased bone and the tendency toward deformity in spite of definite overgrowth. This concept of the disease is applicable to the striking case report of Wycis.<sup>4</sup> Softening of architecturally weak bone has been reported as causing compression of the cord, but his is the first case of platybasia due to Paget's disease in which molding of the bone of the base of the skull caused

4. Wycis, H. T.: Basilar Impression (Platybasia): A Case Secondary to Advanced Paget's Disease with Severe Neurologic Manifestations; Successful Surgical Result, *J. Neurosurg.* **1**: 299-305 (Sept.) 1944.

encroachment on the brain, resulting in severe neurologic symptoms. An unusually good result followed surgical treatment in which laminectomy and suboccipital decompression were done.

*Neurofibromatosis and Osteitis Fibrosa Cystica.*—In an excellent article Thannhauser<sup>5</sup> manifests interest in these conditions. Information continues to be added to the knowledge of them, though in their essential clinical features they are much the same as von Recklinghausen described them. Even he referred to cases with identical features reported by previous authors. The French school, led by P. Marie and H. Bernard, added to the syndrome the pigmentary anomalies of the skin, while the German, English and American literature added the visceral and the osseous changes. Mandl contributed a great advancement in knowledge when he described extirpation of an adenomatous parathyroid gland from a patient suffering from osteitis fibrosa cystica. Knowledge was also added by the physiologic studies of Collip.

Thannhauser clarifies the pathogenesis of osteitis fibrosa cystica localisata and disseminata (von Recklinghausen) and demonstrates that under the heading of osteitis fibrosa cystica Recklinghausen two etiologically different entities are reported: Osteitis fibrosa cystica disseminata is shown to be related by its clinical and histologic features to neurofibromatosis (Recklinghausen); hyperparathyroidism with resulting fibrocystic lesions of bone is primarily caused by hyperfunction or adenoma of one or both parathyroids.

Coburn<sup>6</sup> emphasizes that in cases of parathyroid adenoma the diagnosis is often overlooked and states that this is regrettable because of the brilliant results from early extirpation. He reports a case in detail in which symptoms were manifest over a period of fifteen years.

Ordinarily, after removal of a parathyroid adenoma, the skeleton lesions recalcify. Voltz and Smull<sup>7</sup> report a case, however, in which in five postoperative years this failed to occur, though there was no recurrence of hyperparathyroidism.

5. Thannhauser, S. J.: Neurofibromatosis (von Recklinghausen) and Osteitis Fibrosa Cystica Localisata et Disseminata (von Recklinghausen), *Medicine* 23:105-149 (May) 1944.

6. Coburn, D. E.: Severe Osteitis Fibrosa Cystica with Parathyroid Tumor, *Am. J. Surg.* 66:252-258 (Nov.) 1944.

7. Voltz, C. P., and Smull, K.: Hyperparathyroidism with Failure to Recalcify After Removal of Parathyroid Adenoma (A Case Report), *Ann. Int. Med.* 21:329-332 (Aug.) 1944.

Alexander, Pemberton, Kepler and Broders<sup>8</sup> summarize completely most of the knowledge of parathyroid tumors to date. They report 14 cases and lay stress on the widely divergent clinical pictures. It is brought out that the changes in bone appear to be an index more of duration than of severity.

*Osteomalacia.*—Ghormley and Hinchey<sup>9</sup> suggest the use of aluminum acetate in treatment of malacic bone diseases. They present clinical cases of improvement in symptoms and roentgenologic evidence of increase in calcification as justification for its clinical trial and as a stimulus to research. A high percentage of improvement was noted in cases of osteoporosis, osteitis deformans, osteitis fibrosa and osteogenesis imperfecta.

The incidence of renal lithiasis in this series was 60 per cent. In 13, or 92.8 per cent, of the cases, the tumor showed cytologic evidence of malignancy. The malignant nature of the tumors makes complete removal imperative, according to the authors. It is therefore not advisable to leave tissue to avoid tetany, as this condition can be controlled with calcium and vitamin D.

*Fibrous Dysplasia of Bones (Albright Syndrome).*—Dockerty, Meyerding and Wallace<sup>10</sup> report the thirty-fourth case in the literature since the description of fibrous dysplasia of bones in 1937 by Albright. In the case presented there was the characteristic triad of rather dissociated manifestations, consisting in disseminated fibrosis of bone, patchy cutaneous pigmentation and precocious puberty in females.

*Osteogenesis Imperfecta.*—For some time, discussion has centered around the question as to whether osteogenesis imperfecta (Vrolik), in which there are intrauterine fractures, differs from the Lobstein type, in which only postnatal fractures occur. Rosenbaum<sup>11</sup> reports cases of the two types in the same family, tending to disprove the duality of the syndromes as propounded by Glanzmann. In addition, he found

8. Alexander, H. B.; Pemberton, J. deJ.; Kepler, E. J., and Broders, A. C.: Functional Parathyroid Tumors and Hyperparathyroidism, *Am. J. Surg.* 65: 157-188 (Aug.) 1944.

9. Ghormley, R. K., and Hinchey, J. J.: The Use of Aluminum Acetate in the Treatment of Malacic Diseases of Bone, *J. Bone & Joint Surg.* 26:811-817 (Oct.) 1944.

10. Dockerty, M. D.; Meyerding, H. W., and Wallace, G. T.: Albright Syndrome (Fibrous Dysplasia of Bones, with Cutaneous Pigmentation in Both Sexes and Gonadal Dysfunction in Females), *Proc. Staff Meet., Mayo Clin.* 19:81-88 (Feb. 23) 1944.

11. Rosenbaum, S.: Osteogenesis Imperfecta and Osteopsathyrosis, *J. Pediat.* 25:161-167 (Aug.) 1944.



on laboratory analysis that the values for serum calcium and inorganic phosphorus fluctuate in the course of the disease and fail to form a basis of distinction between the two types. The author postulates a common pathogenesis, implicating the hypophysis and advises treatment with anterior pituitary extract, as it has given good results in his cases.

**Leprosy and Yaws.**—Several interesting reports on these rather unusual diseases have been made. Cooney and Crosby<sup>12</sup> state that in leprosy absorption of bone, particularly in the phalanges, is frequently observed. Case reports and roentgenograms are presented, and the authors state that all the factors for absorption of bone are present, namely, disturbances of circulation, anesthesia and pressure. They believe that these factors working together without any other lytic agent are sufficient to cause the absorption and disappearance of bones.

Faget and Mayoral,<sup>13</sup> in reviewing 505 cases of leprosy, found that osseous changes are found preponderantly in the neural type and are neurotrophic in nature. They are not characteristic but are similar to and essentially indistinguishable from other neurotrophic conditions. Osseous lesions in lepromatous leprosy are rare. These changes are due to involvement of the bone marrow or periosteum by the Hansen bacilli or to a vascular leprosy of the supplying arteries, in contradistinction to the neural type, which is purely neurotrophic and not due to the bacillus.

Helfet<sup>14</sup> reports that yaws is the most common disease of bone in the tropics. While textbooks liken it to syphilis and most descriptions are of the chronic lesions, the author feels that yaws is more acute. The Wassermann test, however, invariably elicits a positive reaction, and the clinical response to arsenicals is dramatic.

**Growth and Regeneration of Bone.**—Bourne<sup>15</sup> states that many workers have attempted to show experimentally, or simply by speculation, that one or another of the various bone elements has to do with regeneration. The most important role has been variously ascribed to osteo-

cytes (Cohn and Mann); connective tissue of callus (Leriche and Policard); osteoblasts (Keith, Girdlestone and Harris); periosteum (Hertz), and latterly, endosteum and periosteum (Urist and McLean). The author, because of the difficulty of obtaining identical fractures, has studied regeneration in bones (femoral and cranial) in guinea pigs and rats. His work corroborates the belief that endosteum and periosteum play an important part in regeneration. He also concludes that regeneration of bone is impaired by a deficiency of ascorbic acid.

Finkler, Furst and Klein<sup>16</sup> report studies of 81 children treated with endocrine substances: 18 with thyroid; 26 with anterior pituitary extract; 19 with chorionic gonadotropin, and 18 with testosterone propionate. They conclude that thyroid therapy tended to improve density of bone and epiphyseal union. Therapy with anterior pituitary extract failed to yield conclusive changes in skeletal and growth development. Chorionic gonadotropin stimulated growth of bone in the longitudinal axis but did not accelerate epiphyseal union or density of bone. Testosterone showed a tendency to accelerate skeletal growth to a greater degree than chorionic gonadotropin. No hastening of epiphyseal union was observed. A moderate degree of increased density of bone was noted, however, in 3 of 18 children.

Reynolds<sup>17</sup> attempts to determine whether there is a greater similarity in the pattern of appearance of certain ossification centers in related than in unrelated children. Twins, siblings, first cousins and unrelated children were used in the study. The conclusion was that patterns are more similar the more closely the children are related. Heredity is implicated as the probable reason.

In a study of seasonal differences in weight, height and appearance of ossification centers in 133 children during the age span from 12 to 60 months, Reynolds and Sontag<sup>18</sup> conclude that seasonal variations, similar in the two sexes, occur as follows: in weight, pronounced; in ossification, moderate, and in height, slight. The authors feel that analyses of deviations in individual growth curves should take into consideration the season of the year which is covered by the interval between measurements.

12. Cooney, J. P., and Crosby, E. H.: Absorptive Bone Changes in Leprosy, *Radiology* 42:14-19 (Jan.) 1944.

13. Faget, G. H., and Mayoral, A.: Bone Changes in Leprosy: A Clinical and Roentgenologic Study of 505 Cases, *Radiology* 42:1-13 (Jan.) 1944.

14. Helfet, A. J.: Acute Manifestations of Yaws of Bone and Joint, *J. Bone & Joint Surg.* 26:672-681 (Oct.) 1944.

15. Bourne, G. H.: The Relative Importance of Periosteum and Endosteum in Bone Healing and the Relationship of Vitamin C to Their Activities, *Proc. Roy. Soc. Med.* 37:275-279 (April) 1944.

16. Finkler, R. S.; Furst, N. J., and Klein, M.: Clinical and Roentgenologic Study of Effects of Hormone Therapy on Bone Growth, *Radiology* 43:346-357 (Oct.) 1944.

17. Reynolds, E. L.: Degree of Kinship and Pattern of Ossification, *Am. J. Phys. Anthropol.* 1:405-415 (Dec.) 1943.

18. Reynolds, E. L., and Sontag, L. W.: Seasonal Variations in Weight, Height and Appearance of Ossification Centers, *J. Pediatr.* 23:524-535 (May) 1944.

Holm<sup>19</sup> calls attention to the lines formed in growing bones as a result of phosphorus poisoning and shows by roentgenograms that they may last a lifetime.

*Ligaments, Muscles and Tendons.*—Kuhns<sup>20</sup> points out that ligamentous weakness is present and easily discernible as a clinical entity in 10 per cent of children but that ligamentous tightness is also present in many and has received scant attention. Tightness is found more frequently in the hamstring and back areas.

Goldberg and Comstock<sup>21</sup> emphasize the differential diagnosis of herniations of muscle observed in the legs from lipoma, hematoma, tuberculosis, pseudo hernia and varices. A case of multiple small hernias of the tibialis anterior muscles of both legs is presented.

In an analysis of 190 cases of chronic non-specific tenosynovitis and peritendinitis, Lipscomb<sup>22</sup> feels that trauma is in most instances the etiologic factor. The pathologic changes are reviewed, and his opinion is that they differ only in degree and depend on the duration of the disease primarily. Conservative treatment consisting in splinting and roentgen ray therapy is advised, and if improvement does not occur surgical intervention is indicated.

19. Holm, O. F.: Beitrag zur Kenntnis der Entstehung der Phosphorsklerose, *Acta radiol.* **23**:549-561, 1942.

20. Kuhns, J. G.: Tightness of Ligamentous Structures, *Arch. Pediat.* **61**:179-183 (April) 1944.

21. Goldberg, H. C., and Comstock, G. W.: Herniation of Muscles of the Legs, *War Med.* **5**:365-367 (June) 1944.

22. Lipscomb, P. R.: Chronic Nonspecific Tenosynovitis and Peritendinitis, *S. Clin. North America* **24**:780-797 (Aug.) 1944.

*Osteochondritis.*—Uhry<sup>23</sup> presents an interesting review of 79 cases of osteochondrosis of the tuberosity of the tibia (Osgood-Schlatter's disease) and defends the original ideas of the persons first describing the condition in which the disorder develops as a result of minor separation of the structures of the tibial tubercle and the patellar ligament. The author believes that the characteristic pathologic changes represent callus repair at the site of separation. He feels that osteochondritis as such (that is, inflammation) is not in evidence. The immediate instigating factor is consistently trauma.

*Sudeck's Atrophy.*—Buchman<sup>24</sup> reports an interesting case of Sudeck's atrophy following a single minor surgical procedure for exploration of a tendon sheath. The surgical treatment was followed by severe symptoms, partially relieved by injection of procaine hydrochloride after lack of response to usual methods of treatment.

*Abuse of Bed Rest.*—Since this article will probably not come within the purview of the editors of other sections of "Progress in Orthopedic Surgery," it is felt that it should be mentioned here. Ghormley<sup>25</sup> sounds a keynote of change from the emphasis placed on rest by Hugh Owen Thomas and cites the many disadvantages of rest as compared with early activity in the orthopedic field.

23. Uhry, E., Jr.: Osgood-Schlatter Disease, *Arch. Surg.* **48**:406-414 (May) 1944.

24. Buchman, J.: Postoperative Post-Traumatic Osteoporosis or Sudeck's Atrophy, *Bull. Hosp. Joint Dis.* **4**:55-61 (Oct.) 1943.

25. Ghormley, R. K.: Abuse of Rest in Bed in Orthopedic Surgery, *J. A. M. A.* **125**:1085-1087 (Aug. 19) 1944.

## II. CONGENITAL DEFORMITIES

PREPARED BY J. HIRAM KITE, M.D., ATLANTA, GA.

For several years I have begun this section on "congenital deformities" with a description of the experiments conducted by Josef Warkany. Each year he and his workers have given additional information on the cause of some of the congenital deformities. This past year has brought information on how to prevent deformities.

In times past, various authors have attributed congenital malformations to a maternal nutritional deficiency. Warkany and Schraffenberger,<sup>26</sup> after establishing a set pattern of deformities which follow what they call diet I, made

various additions to the diet, trying to prevent deformities. They found first that 2 per cent pig liver would prevent deformities. A search was made for the preventive factor in pig liver. After studying hundreds of litters of rats, they give the following conclusions:

The congenital malformations of the pattern of diet I are prevented when the maternal diet I is supplemented by riboflavin. Supplements of thiamine hydrochloride, nicotinic acid, pyridoxine and calcium pantothenate are not preventive. With a purified maternal diet in which the vitamin B complex is represented by crystalline substances, malformations of the pattern of diet I appear in the offspring when riboflavin is omitted. On the same diet supplemented by

26. Warkany, J., and Schraffenberger, E.: Congenital Malformations Induced in Rats by Maternal Nutritional Deficiency, *J. Nutrition* **27**:477 (June) 1944.

sufficient riboflavin, no deformed offspring are observed. It is concluded that a deficiency of riboflavin in the maternal diet is responsible for the congenital malformations of the pattern of diet I.

The late Beveridge H. Moore<sup>27</sup> gave further insight into congenital deformities by his study of peripheral nerve changes. He found that one or the other of the parents of a child showing the congenital malformation will frequently show definite stigmas of neurofibromatosis, even though the child himself does not. The pigmentation may not be seen in the child, but it makes its appearance later. He found in 2 cases of amputation for hypertrophy that there were nodules along the peripheral nerves. Some of the nodules showed changes typical of neurofibroma, while others showed a variety of changes. He studied the nerve between the nodules, where it was supposed to be normal, and found many secondary changes, a fact which he thinks is extremely important. The basic change is an increase in the fibrous tissue of the endoneurium. He calls these changes fibrotic degeneration. It is believed that they are either an early stage in the formation of a neurofibromatous nodule or an indication of its presence elsewhere in the nerve trunk. He studied all nerves available, those of spastic patients when the nerve was sectioned and those in supernumerary digits and in other deformities requiring amputation. He found that a surprisingly high proportion of this supposedly normal material showed changes corresponding to the secondary pathologic changes which have been referred to as fibrotic degeneration. The striking feature of the study was the high percentage of cases of pathologic changes in nerves and their relationship to the cutaneous pigmentation considered typical of pathologic changes of nerves. In a high percentage of congenital deformities varying degrees of pathologic changes in the peripheral nerves are shown. This observation seems to favor the neurogenic theory of the origin of congenital deformities.

Sections of peripheral nerves from 78 cases of various congenital deformities were studied with regard to disease. Of the 78 cases, 70, or 91 per cent, showed pathologic changes in the nerves.

[ED. NOTE (L. D. B.).—Beveridge Moore, a fine gentleman, in his studies of peripheral nerve lesions made a major contribution to orthopedic surgery.]

27. Moore, B. H.: Peripheral Nerve Changes Associated with Congenital Deformities, *J. Bone & Joint Surg.* 26:282 (April) 1944.

Two cases of multiple congenital deformities are reported by Hobbs.<sup>28</sup> These are used as the basis for a discussion of the hereditary factors in multiple congenital deformities. The literature is reviewed. The experiments concerning inheritable deformity in animals through injury to the gonads by roentgen rays have given rise to the supposition among students of genetics that the clinical use of roentgen rays may be responsible for congenital deformities in human progeny. Such disorders cannot be entirely charged to roentgen ray injury, nor can such injury be believed to be a principal etiologic factor, since the deformities were commonly observed prior to the era of clinical radiology. The primary cause of clinical as well as experimental produced hereditary deformities can be radiation energy or another agent capable of producing sublethal changes in the primary germ cell.

Swan and others<sup>29</sup> report further observations on congenital defects in infants following infectious diseases during pregnancy, with special reference to rubella. Recent work reported previously showed that maternal rubella in the early months of pregnancy may be followed by congenital defects (cataract, heart disease, deaf-mutism, microcephaly and glomerular sclerosis, in the infants born subsequently. The possibility that other infectious diseases in pregnancy may result in congenital abnormalities has been considered.

In the course of the present investigation, 13 infants were examined; 11 were found to have congenital abnormalities. In 12 instances the mothers had suffered from rubella during pregnancy; 10 of the infants born subsequently exhibited congenital defects. The abnormalities included cataract, deaf-mutism, heart disease, microcephaly and obliteration of the bile ducts. With three exceptions, all 10 mothers with congenitally defective children had contracted rubella within the first three months of pregnancy.

[ED. NOTE (L. D. B.).—This association of congenital deformities with rubella during pregnancy adds further to the interest in the work of Cohn on the study of blood fractions, in that the gamma globulin has been shown to prevent rubeola. Additional studies are indicated to determine its effect on rubella.]

A case of epiphyseal dysgenesis associated with cretinism in a premature infant is reported by

28. Hobbs, A. A.: Hereditary Factors in Multiple Congenital Deformities, *Am. J. Roentgenol.* 51:677 (June) 1944.

29. Swan, C.; Tostevin, A. L.; Mayo, H., and Black, G. H. B.: Further Observations on Congenital Defects in Infants Following Infectious Diseases During Pregnancy, with Special Reference to Rubella, *M. J. Australia* 1:409 (May 6) 1944.

att, Zeldes and Goodfriend.<sup>30</sup> They pointed out that in 1927 Fairbank described "stippled epiphyses" associated with dwarfism, but he failed to recognize thyroid deficiency as the basis of the disturbance. Ten years later Reilly and Smythe described 5 similar cases, designating the condition as "cretinoid epiphysial dysgenesis." McCullough and Sutherland in 1940 described stippled epiphyses in a dwarf in whom there was no sign of hypothyroidism and used the term "epiphysial dysplasia punctularis" to designate the skeletal change. Wilkins, who found bilateral epiphysial dysgenesis in 23 of 25 children with hypothyroidism, said that he had never seen true dysgenesis in any type of dwarfism other than that occurring with hypothyroidism.

In roentgenograms epiphysial dysgenesis is diagnosed by the appearance of multiple small irregular islets of calcification, scattered over a considerable area. The islets are irregularly spaced, and the anatomic distribution does not conform to that of the normal centers of ossification. As the islets grow larger or as new ones occur, they appear to coalesce and give the impression of a single large center which has undergone fragmentation. The defect is apparently due to an abnormality of endochondral ossification.

Roentgenologically, epiphysial dysgenesis may be confused with osteochondritis deformans. However, the latter usually occurs in epiphyses which previously have appeared normal on roentgen examination. Furthermore, osteochondritis deformans (Legg-Calve Perthe's disease, Osgood-Schlatter disease) is usually unilateral, occurring most frequently in only one epiphysis. It is generally accompanied with pain and does not respond to thyroid therapy.

[ED. NOTE (L. D. B.).—Osteochondritis or osteochondrosis is frequently bilateral.]

Achondroplasia fetalis may be confused with cretinism clinically, but the latter may be differentiated by the unique deformities of the metaphyses and shafts of the long bones and the grossly abnormal shapes of the epiphyses.

Carl Badgley<sup>31</sup> advances the theory that the pathogenesis of the multiple deformities occurring in arthrogryposis multiplex congenita may best be explained on the basis of arrest of embryonic development. A primary pathologic change of the muscle, which has been proved

inherent in lambs but which is of unknown origin in human beings, can well be the causative factor of this arrest. The normal rotation of the limb buds, an intrinsic characteristic of the human fetus, is carried out by the muscles of the extremity. The loss of muscle function arrests or prevents this rotation. The resultant club feet, club hands and postural deformities are the retained posture normal for the 3 month fetus but arrested from rotation into the characteristic human attitude. The rigidity of the joints is similarly the result of failure of muscle function, preventing normal fetal motion in otherwise normally developing joints.

Correction of the deformities by release operations to reestablish mobility and to continue rotation of the extremities to the normal posture of mature human extremities is the aim of therapy. The muscular damage is of course irreparable, but pronounced improvement in function can be obtained. Early treatment, with early operative correction of the deformities if necessary, is advised.

[ED. NOTE (L. D. B.).—Attempts at correcting arthrogryposis deformities are sometimes most discouraging.]

Lyons and Sawyer<sup>32</sup> report a case of cleidocranial dysostosis in a veteran of World War I. They say that cleidocranial dysostosis is a comparatively rare congenital defect of the bony skeleton. Less than 100 cases have been reported in the literature. It is a syndrome in which the chief characteristic observation is a complete or partial absence of one or both clavicles. As so often happens, when one congenital defect is found in the body, another may also be found. In this condition one of the more constant defects accompanying that of the clavicles is a variation in the development of the bones of the skull. Barlow in 1883 reported a case of congenital absence of the clavicles and malformation of the cranium in a girl aged 2 years, probably the first typical case described. In 1897 Marie and Sinton reported 4 cases and applied the term "hereditary cleidocranial dysostosis" to the anomaly syndrome. Fitchet in 1929 made a complete survey of all reported cases in the literature. He stated that the chief features of this syndrome are grouped under four headings as follows: aplasia, more or less pronounced, of the clavicles; exaggerated development of the transverse diameter of the cranium; delay in the ossification of the fontanels, and hereditary transmission. Fitchet expressed the belief that the term "hereditary cleidocranial dysostosis" should be discontinued and "congenital cleidal dysos-

30. Blatt, M. L.; Zeldes, M., and Goodfriend, J.: Epiphysial Dysgenesis Associated with Cretinism in a Premature Infant, *Am. J. Dis. Child.* 67:480 (June) 1944.

31. Badgley, C. E.: Rehabilitation in Cases of Arthrogryposis Multiplex Congenita, *Arch. Phys. Therapy* 24:733 (Dec.) 1943.

32. Lyons, C. G., and Sawyer, J. G.: Cleidocranial Dysostosis, *Am. J. Roentgenol.* 51:215 (Feb.) 1944.

tosis" substituted, since the condition may be either hereditary or nonhereditary, with or without other anomalies.

The clavicular deformity may vary from defects at the acromial end to complete absence of one or both clavicles. The latter is unusual, however. Most frequently it is the middle portion of the clavicle that is involved.

The defects of the skull may consist in brachycephalic changes, prominence of the frontal and parietal bosses or delay in closure of sutures and fontanels.

Most of the patients are described as being of small stature. Anomalies of dentition are common, consisting in delay in the appearance of permanent teeth, incompleteness or irregularity of the second set of teeth and a proneness to caries, missing teeth or supernumerary teeth. A high palatal arch is also rather frequent. Defects in the bones of the hands and feet, including shortening of the toes, have also been reported.

Salmon<sup>33</sup> reports another case of hereditary cleidocranial dysostosis in a soldier. In this case the characteristic features were partial aplasia of the clavicles, abnormal mobility of the shoulders, failure of the fontanels to close and defective union of the cranial sutures. The patient's father and sister showed evidences of the disease.

A case of Naeglele pelvis associated with rudimentary femur is reported by Wahrsinger.<sup>34</sup> The patient had a congenital absence of the upper part of the right femur. A knee joint was present, but there was a very rudimentary lower part of the femur. An operation was performed in which the side of the ilium was turned down and the rudimentary femur was brought up against it in order to permit weight bearing of the femur against the side of the ilium. The foot was at the level of the knee, and the patient walked with an artificial limb. The pelvis showed a great deal of asymmetry. The measurements and the roentgenograms suggested that it would hardly be possible for a normal delivery to occur. However, after a total labor of twenty-three hours, the patient was delivered spontaneously of a living 6 pound 14 ounce (3,120 Gm.) girl.

Since the last part of the nineteenth century, there have appeared in the literature isolated reports dealing with the association of malformations of the nails, hypoplasia or complete absence of the patellas and deformities with impaired

function of the elbows. Senturia and colleagues<sup>35</sup> report another case. They state that in many cases this triad has been inherited, in varying modification, in several generations of the family, while in others one or more of the cardinal features have been absent or altered. The deformities are purely inherited or congenital and are apparently due to some developmental defect in the ectodermal and mesodermal layers of the embryo. The triad is transmitted as a hereditary dominant character and is not sex linked. A case is described in which there was the typical clinical and roentgenologic appearance, and in the patient's family tree a total of 30 persons in four generations have been similarly affected.

The clinical and roentgenologic appearance of two congenital deformities of the leg are described by Williams.<sup>36</sup> These are congenital angulation (kyphosis) of the tibia and congenital pseudarthrosis of the tibia (and fibula). He says that the two deformities bear a superficial resemblance in that typically there is a forward angulation or bowing in the lower half of the tibia. The treatment of both conditions is difficult, and the functional outlook is poor. There is probably little direct etiologic association of the two conditions, though the risk of development of pseudarthrosis in the deliberate corrective treatment of congenital angulation is considerable. It would appear likely that in congenital pseudarthrosis the primary defect is one of local failure of osteogenesis. In congenital angulation the primary defect may well be muscular, secondarily affecting the architecture of the bone; however, the functional association of other congenital defects (e. g., absence of the fibula and dislocation of the hip) suggests a basic mesenchymal defect which causes both a limitation of muscular growth and a failure of transitional differentiation to fibrocartilage, cartilage and true bone. Congenital absence of a normal bony structure should not be inferred from roentgenographic examination, since a structure may well be formed in cartilage though lacking in ossification.

[ED. NOTE (L. D. B.).—Beveridge H. Moore has shown a definite association between neurofibromatosis and congenital angulation and pseudarthrosis of the tibia, and his observations have been confirmed by many investigators.]

35. Senturia, H. R., and Ben, D.: Congenital Absence of the Patellae Associated with Arthrodysplasia of the Elbows and Dystrophy of the Nails, *Am. J. Roentgenol.* 51:352 (March) 1944.

36. Williams, E. R.: Two Congenital Deformities of the Tibia: Congenital Angulation and Congenital Pseudarthrosis, *Brit. J. Radiol.* 16:371 (Dec.) 1943.

33. Salmon, D. D.: Hereditary Cleidocranial Dysostosis, *Radiology* 42:391 (April) 1944.

34. Wahrsinger, P. B.: Naeglele Pelvis Associated with Rudimentary Femur, *Am. J. Obst. & Gynec.* 47:427 (March) 1944.

bell and Grice,<sup>37</sup> from Boston, describe their modification of the Denis Browne splint for the treatment of congenital club feet. They use a splint which is narrower in the heel and makes the foot better and is also arched to prevent the heel from sinking under the foot. They have made an improvement in the method of strapping the foot to the splint. They give the following summary:

During the treatment of 53 patients with complicated congenital talipes equinovarus with the modified Denis Browne splint, several refinements in technic have been evolved to meet various problems, such as pressure sores, dermal ulcers, incomplete correction, persistent equinus deformity, loss of longitudinal arch and unilateral deformity. These refinements are described. Success of this method depends on the accuracy with which the foot is fixed to the splint. If properly applied, the splints will allow correction

37. Bell, J. F., and Grice, D. S.: Treatment of Congenital Talipes Equinovarus with the Modified Denis Browne Splint, *J. Bone & Joint Surg.* 26:799 (Oct.) 1944.

of the varus deformity and yet will maintain the longitudinal arch while obtaining full correction of the equinus deformity. Recurrence of the deformity is a constant threat, but this tendency is minimized by complete correction early and then by continued use of the splint intermittently, at least until the child begins to walk.

[ED. NOTE (J. H. K.).—For the last two years I have commented at length on my experiences with the Denis Browne splint. Briefly, I have obtained better results with plaster. I have tried the method of strapping mentioned by the author and feel that it is an improvement. Denis Browne says that he has made more than fifty modifications of the splint. Still more may be expected.]

[ED. NOTE (L. D. B.).—I have seen Grice apply the modified splint and have seen several of the patients. The splint and the method of applying the adhesive are great improvements in the Denis Browne technic, and any one using splint therapy should adopt these modifications.]

### III. TUMORS OF BONE AND OF SYNOVIAL MEMBRANE

PREPARED BY HENRY W. MEYERDING, M.D., ROCHESTER, MINN.

A. *Classification of Tumors of Bone.*—Brachetto-Brian<sup>38</sup> presents a classification adopted by the "Comité para el Estudio de los Tumores Oseos" of the Asociación Argentina de Cirugía.

He discusses various phases and believes that the classification should be based on the type of tissue affected, since different cells would originate different neoplasms. The classification is as follows:

	Genetic Cells	Neoplasms Originated	Names of Tumors
A. Tumors of the skeletal sector	Osteoblast	I. Osteoblastoma	Benign Malignant Osteoma Osteosarcoma; osteogenic sarcoma
	Chondroblast	II. Chondroblastoma	Benign Malignant Chondroma Chondrosarcoma
	Myeloplax	III. Myeloplaxoma	Benign Malignant Giant cell tumor
B. Tumors of the reticulo-endothelial sector	Mesoblast Histioocyte Reticuloblast Angioblast	IV. Reticuloblastoma	Benign Malignant Reticulosarcoma Ewing's sarcoma
C. Tumors of the hematopoietic sector	Mesoblast Hemoblastioblast Hemocytoblast	V. Myeloblastoma	Kahler's disease; myeloma
D. Tumors of the vasculo-connective sector	Mesoblast Fibroblast Angioblast	VI. Fibroma and so forth	Benign
		VII. Osteosarcoma	Malignant

In the following tabulation these seven groups of neoplasms are represented with their varieties:

A. Tumors of the skeletal sector	I. Osteoblastoma	Benign	1. Benign osteoblastoma of the substantia spongiosa 2. Benign sclerosing osteoblastoma 3. Benign chondro-osteoblastoma
		Malignant	1. Malignant osteogenic osteoblastoma 2. Malignant osteogenic osteoblastoma with myeloplaxes 3. Secondary malignant osteogenic osteoblastoma 4. Juxtaconjugal malignant osteogenic osteoblastoma 5. Telangiectatic malignant osteogenic osteoblastoma
	II. Chondroblastoma	Benign	1. Chondroblastoma 2. Chondromyxoblastoma
		Malignant	1. Malignant chondroblastoma 2. Malignant myeloplaxoma
B. Tumors of the reticulo-endothelial sector	III. Myeloplaxoma	Benign	1. Benign myeloplaxoma 2. Malignant myeloplaxoma
		Malignant	1. Localized reticuloendothelioma
	IV. Reticuloblastoma	Benign	1. Undifferentiated reticulosarcoma
		Malignant	2. Differentiated reticulosarcoma

38. Brachetto-Brian, D.: La clasificación adoptada en el "comité para el estudio de los tumores oseos." *Rev. Prensa méd. argent.* 28:2185-2190 (Nov. 19) 1941;

abstracted, *Arch. cubanos cancerol.* 3:19-26 (Jan.-March) 1944.

O. Tumors of the hemopoietic sector  
D. Tumors of the vascular-connective sector

V. Myeloblastoma

Solitary  
Multiple

VI. Fibroma and so forth .....

VII. Osteosarcoma .....

1. Plasmocellular myelosarcoma
1. Plasmocellular myelosarcoma
2. Myeloblastic myelosarcoma
1. Fibroma
2. Lipoma
3. Osteolipoma
4. Myxoma
5. Angioma
1. Fibroblastic osteosarcoma
2. Myxoblastic osteosarcoma
3. Lipoblastic osteosarcoma
4. Angioblastic osteosarcoma

### B. Lesions Simulating Neoplasms of Bone.—

Echternacht<sup>39</sup> presents a case of hemophilia in which the patient injured the tibia. Following the injury, there was tumefaction, with roentgenographic evidence of destruction of bone suggestive of a malignant lesion. Roentgen therapy was given, and later amputation was done through the knee joint, followed by hemorrhage and fatal termination.

Friedman<sup>40</sup> presents 4 cases of neurofibromatosis with involvement of bone. In 1 case, material obtained for biopsy from the medullary canal of the femur contained neurofibromatous tissue. He suggests that there is normally some nervous tissue present in bone marrow.

Kleinberg<sup>41</sup> presents a case of solitary bone cyst of the neck of the left femur in which slow progression was noted roentgenologically for a period of twenty years and in which a cure was effected by opening and curetting the cavity and packing it with bone chips.

[ED. NOTE.—The destruction of the wall of the cyst will produce bleeding and promote formation of bone, but we believe that more rapid healing occurs if the cavity is packed with bone chips than if this is not done.]

Faust, Gilmore and Mudgett<sup>42</sup> have made a good review of the literature on chondromas, including embryology, histology and clinical picture. They present a case of a large malignant sacrococcygeal chondroma with metastasis and fatal termination.

Pavlovsky, Paterson Toledo and Muscolo<sup>43</sup> review the literature and present a series of 25 cases in which the patients had secondary invasion of bone with lymphogranulomatosis:

39. Echternacht, A. P.: Pseudotumor of Bone in Hemophilia, *Radiology* **41**:565-572 (Dec.) 1943.
40. Friedman, M. M.: Neurofibromatosis of Bone, *Am. J. Roentgenol.* **51**:623-630 (May) 1944.
41. Kleinberg, S.: The Solitary Bone Cyst: A Report of a Case of Twenty Years' Duration, *J. Bone & Joint Surg.* **26**:337-343 (April) 1944.
42. Faust, D. B.; Gilmore, H. R., Jr., and Mudgett, C. S.: Chordomata: Review of Literature, with Report of Sacrococcygeal Case, *Ann. Int. Med.* **21**:678-698 (Oct.) 1944.
43. Pavlovsky, A.; Paterson Toledo, R., and Muscolo, D.: Linfogranulomatosis ósea: comentarios sobre 25 observaciones, *Rev. ortop. y traumatol.* **13**:136-157 (Jan.) 1944.

Thoma<sup>44</sup> presents a case of eosinophilic granuloma with diabetes insipidus in which the patient received roentgen therapy that practically healed the lesions of the mandible and in which posterior pituitary controlled the diabetes insipidus. This is the first case of eosinophilic granuloma with diabetes insipidus that has been reported, and in Thoma's mind the case links this condition more strongly with Schüller-Christian disease.

Jaffe and Lichtenstein<sup>45</sup> present another review of eosinophilic granuloma of bone, the previous one having been presented in 1940. They feel that it is apparently an inflammatory reaction to some unknown agent and may be single or multiple. Microscopically the cystic or granulomatous lesion shows an abundance of histiocytes and eosinophilic cells. The lesions may resolve without therapy of any kind or may heal after simple curettage. The differences and simulations between eosinophilic granuloma, Letterer-Siwe disease and Schüller-Christian disease of bone are outlined.

Osborne, Freis and Levin<sup>46</sup> point out that no case of eosinophilic granuloma of bone with neurologic signs or symptoms has been reported previously. They present a case of this condition, in which the complaint was paralysis of the left side of the face and later vertigo and nausea. There was roentgenologic evidence of destructive lesions of the left temporal bone, mandible, vertebrae, ribs and right femur. A biopsy was done on the mandible and the fifth rib, and examination of the tissue revealed changes typical of granuloma. Roentgen therapy was given, with complete subsidence of the neurologic signs and

44. Thoma, K. H.: Eosinophilic Granuloma with Report of One Case Involving First the Mandible, Later Other Bones, and Being Accompanied by Diabetes Insipidus, *Am. J. Orthodontics (Oral Surg. Sect.)* **29**:641-651 (Dec.) 1943.
45. Jaffe, H. L., and Lichtenstein, L.: Eosinophilic Granuloma of Bone: Condition Affecting One, Several or Many Bones, but Apparently Limited to Skeletal and Representing Mildest Clinical Expression of Pectus Inflammatory Histiocytosis also Underlying Letterer-Siwe Disease and Schüller-Christian Disease, *Arch. Path. & Bact.* **37**:99-118 (Feb.) 1944.
46. Osborne, R. L.; Freis, E. D., and Levin, A. G.: Eosinophilic Granuloma of Bone Presenting Neurologic Signs and Symptoms: Report of Case, *Arch. Neurol. & Psychiat.* **51**:452-456 (May) 1944.

symptoms, as well as partial recalcification of some of the defects of bone.

Henschen<sup>47</sup> reports a case of eosinophilic granuloma, in which excision of the lesion from the left mandible of a man 24 years of age was done, followed by recurrence and second operation. He feels that every destructive lesion of bone in adolescents should be suspected of being eosinophilic granuloma.

Cavalcanti<sup>48</sup> reviews the literature on post-traumatic epidermoid cysts and presents a case in which there was involvement of a phalanx of the right middle finger. The lesion was excised and found to be a typical epidermoid cyst on examination.

Pohlmann and Wachstein<sup>49</sup> mention that epidermoid (squamous epithelial) bone cyst of the phalanges, a rare tumor of bone, has been reported as proved in only 10 cases. They present a review of the 10 cases in the literature and an additional case of their own and advocate removal of the cyst and cauterization of the cavity, measures which preserve the finger and prevent possible recurrence of the lesion.

*C. Lesions of Synovial Membrane.*—Moretz<sup>50</sup> reports 4 cases of malignant tumors arising from synovial membrane. He mentions that this type of lesion is classified according to the microscopic picture. Some lesions apparently arise from the outer layers of the synovial tissue and are indistinguishable from fibrosarcoma, and the others arise from the inner layers, thus presenting a more epithelioid type. Both types of tumor cells may be present in the same lesion. The prognosis in any case is unfavorable. Amputation is recommended except in those cases in which conditions are favorable for a wide local excision of the lesion or in those in which there is local recurrence.

*D. Benign Neoplasms of Bone.*—Osteoid osteoma: Stauffer<sup>51</sup> presents a case of osteoid osteoma, in which the lesion was excised from the head of the radius, with complete relief of symptoms. The previous pathologic report had been "healing benign giant cell tumor."

47. Henschen, C.: Das eosinophile Granulom des Knochens, Schweiz. med. Wchnschr. 73:451-455 (April 10) 1943.

48. Cavalcanti, J.: Cisto epidermoide post-traumático de dedo, Arq. brasil. de cir. e ortop. 11:36-41, 1943.

49. Pohlmann, H. F., and Wachstein, M.: Epidermoid (Squamous Epithelial) Bone Cyst of Phalanx, Ann. Surg. 119:148-154 (Jan.) 1944.

50. Moretz, W. H.: Malignant Tumors Arising from the Synovial Membrane with Report of Four Cases, Surg., Gynec. & Obst. 79:125-132 (Aug.) 1944.

51. Stauffer, H. M.: Osteoid-Osteoma of the Head of the Radius: Case Report, Am. J. Roentgenol. 52: 200-202 (Aug.) 1944.

Harmon<sup>52</sup> presents a case of osteoid osteoma. The patient was a girl 9 years of age, and the lesion was located in the midportion of the femoral shaft. All laboratory tests gave normal results. At operation a soft gritty material was found in the cavity. Cultures revealed no growth. The microscopic examination revealed osteoid tissue between hypertrophic trabeculae with fibrous reaction and no inflammatory cells.

Kleinberg<sup>53</sup> reports 3 cases of osteoid osteoma, one lesion being located in the upper end of the fibula, one involving the lamina of the second lumbar vertebra and one in the neck of the astragalus. He states that the patients had complete relief of all symptoms following excision of the lesion.

Lewis<sup>54</sup> presents 11 cases of osteoid osteoma, in 9 of which the condition was proved and in 2 probably proved. The lesions conformed to the clinical and roentgenologic criteria of Jaffe and Lichtenstein. He advocates simple block removal of the nidus or focus of infection and feels that failure to remove all of this may cause persistence of the symptoms.

[ED. NOTE.—Such case reports as the foregoing are of increasing value and interest to physicians. Jaffe and Lichtenstein have incited a great deal of interest among surgeons, especially orthopedic surgeons, through their studies of this condition. An increasing number of case reports are evident in the literature. In the past the lesion was considered a focus of infection described as nonsuppurative osteomyelitis of Garré, Brodie's abscess or localized subcortical abscess of bone. There still exists among surgeons and pathologists a difference of opinion regarding the lesion.]

Periosteal Fibroma: Sgroso<sup>55</sup> presents a case in which the patient was an 11 year old boy and the huge lesion involved the humerus. Operation had been performed unsuccessfully three months prior to the patient's admission to the hospital. The huge fibroma was removed with good results, a rare condition.

Periosteal Lipoma: Cottini<sup>56</sup> presents a case of periosteal lipoma of the radius, the patient being

52. Harmon, P. H.: Osteoid Osteoma of Mid-Shaft Region of Femur, Am. J. Surg. 66:128-131 (Oct.) 1944.

53. Kleinberg, S.: Osteoid Osteoma, Am. J. Surg. 66:396-401 (Dec.) 1944.

54. Lewis, R. W.: Osteoid-Osteoma: A Review of Portions of the Literature and Presentation of Cases, Am. J. Roentgenol. 52:70-79 (July) 1944.

55. Sgroso, J. A.: Fibroma perióstico del húmero, Rev. ortop. y traumatol. 13:198-204 (April) 1944.

56. Cottini, C. F.: Consideraciones sobre un caso de lipoma perióstico de radio, Bol. y trab., Soc. argent. de cirujanos 4:700-707, 1943; abstracted, Rev. Asoc. méd. argent. 57:995-997 (Nov. 30) 1943.



a girl of 19 years. The lesion had been present for eight years, and the roentgenographic examination revealed a uniformly transparent, sharply delimited area contiguous to the upper third of the radius. The bone appeared normal. The tumor and the involved periosteum were removed. Cottini reviews the literature on this subject and states that periosteal lipoma is most commonly located in the skull.

**E. Giant Cell Tumor.**—Brachetto-Brian<sup>57</sup> presents a review of all the original reports concerning giant cell tumor in an attempt to clarify the nature of the lesion and its characteristics and to establish the relative value of the varied and confusing names that have been applied to this tumor. He proposes the name "myeloplaxoma" as the most appropriate etymologically, historically and biologically. He further proposes that Robin and Eugene Nélaton be duly recognized as the original describers of the lesion.

Samson<sup>58</sup> reports a case of giant cell tumor. The patient was a woman 24 years of age. The lesion appeared in the distal end of the radius. It was successfully resected, and the resulting defect was repaired by means of massive bone grafts. He describes the methods of treating giant cell tumor.

**F. Vascular Neoplasms.**—Anderson<sup>59</sup> states that the orthodox treatment of simple angioma and cavernous angioma should be discarded and roentgen treatment should not be given until the neoplasms reach full growth, at the age of 1 year, since some completely regress before the sixth year of life.

Sherman<sup>60</sup> reports a case of capillary hemangioma of the lower end of the femur. The affected extremity was longer than its fellow, and a roentgenogram revealed an area of radiolucency in the lower end of the femur. At operation, some periosteal reaction was found, and the medullary cavity contained sclerotic cancellous bone.

Maynard<sup>61</sup> states that hemangiomas may grow tremendously large and constitute a major problem and that all angiomas that are sensitive to

radiation should be treated from the day they are discovered, provided they show any tendency to grow.

Kulchar<sup>62</sup> states that tumors of the foot, like those of the hand, are frequently multiple and discusses nine types: 1. Angiomas are mainly congenital. He describes them from the anatomic and histopathologic point of view. Many of them undergo involution spontaneously over a course of years. Angiomas of the cavernous type are treated by roentgen therapy, radium or a sclerosing substance. 2. Tumors of the angioblastoma group (sarcoma) are best treated by excision or irradiation. 3. Angioneuroma, or glomus tumor, was found present in the foot in a third of the cases and was treated by excision or electrocoagulation. 4. Kaposi's sarcoma is treated by irradiation but usually recurs. 5. Ganglion is treated by excision. 6. Fibroma is treated by excision. 7. Melanoma is relatively uncommon. 8. Carcinoma is relatively uncommon. Fibrosarcoma is the commonest form of sarcoma. It is diagnosed by biopsy and is treated by excision or amputation at the junction of the upper third with the lower two thirds of the leg.

[ED. NOTE.—It should be remembered that these vascular neoplasms may be benign or malignant, and it is important that this differentiation be made. I have seen patients who have had prolonged roentgen therapy without appreciable benefit, in whose cases complete excision could have been performed successfully at an earlier stage. When the tumor is so situated and is of such size that surgical excision is impossible, then I feel that roentgen therapy should be given. Furthermore, I have operated on patients with arteriovenous fistula, in whose cases the clinical diagnosis and treatment had been for the vascular tumors.]

**G. Malignant Osteogenic Sarcoma.**—Meyering<sup>63</sup> presents a rare case in which the patient had multiple metatarsal fractures and osteogenic sarcoma. The osteogenic sarcoma was apparently superimposed on the fracture of the second metatarsal bone. Operation had been previously performed for a nasal lesion, and a diagnosis of spindle cell sarcoma had been made. The histologic study of the tumor of the second metatarsal bone was a metastatic lesion. The mother of the patient demanded that surgical excision be carried out. This was accordingly done, after

57. Brachetto-Brian, D.: *Sobre la historia del mieloplaxoma de los huesos; tumor de Robin-Eug. Nélaton*, Rev. Asoc. méd. argent. 57:661-669 (Sept. 15) 1943.

58. Samson, A.: *Traitement des tumeurs à cellules géantes du radius; résection et transplantation osseuse*, Union méd. du Canada 73:30-36 (Jan.) 1944.

59. Anderson, C. R.: *Tumors of the Foot*, J. A. M. A. 125:302 (May 27) 1944.

60. Sherman, M. S.: *Capillary Hemangioma of Bone*, Arch. Path. 38:158-161 (Sept.) 1944.

61. Maynard, M. T.-R.: *Benign and Malignant Tumors of the Foot*, J. A. M. A. 125:990 (Aug. 5) 1944.

62. Kulchar, G. V.: *Benign and Malignant Tumors of the Foot*, J. A. M. A. 124:761-766 (March 15) 1944.

63. Meyering, H. W.: *Multiple Metatarsal Fractures Associated with Osteogenic Sarcoma*, J. A. M. A. 124:228-230 (Jan. 22) 1944.

which the pathologic report was osteosarcoma. Subsequent to this, fracture of the third metatarsal bone with callus formation developed. Excision was again requested, and the lesion proved to be benign march fracture with callus formation. Still later the patient had fractures of the first and fourth metatarsal bones, which were evident on roentgenographic examination. At the time the paper was written, he was living and working in a lumber mill fourteen years following operation on the second metatarsal bone. The specimen and the tissues were reexamined by Dr. Broders and showed unquestionably that the original lesion of the second metatarsal bone was osteosarcoma and that the lesion of the third metatarsal bone was march fracture.

Gershon-Cohen and Doran<sup>64</sup> review the literature of fatigue-stress fractures and emphasize the necessity for ruling out systemic disease and local pathologic changes. They support the hypothesis of fatigue-stress and present 4 cases. They state that the fracture lines are thin and the callus formation is diagnostic, although they believe that the lesion could be taken for osteogenic sarcoma in the latter stages of the condition.

[ED. NOTE.—My case reported at the beginning of this section illustrates the confusion which could arise by depending on roentgen interpretation alone.]

Friedman<sup>65</sup> reports a case of osteolytic osteogenic sarcoma of the os pubis, which is an extremely rare location. His patient was a woman 42 years of age. Roentgenographic examination revealed destruction of the right horizontal ramus of the pubic bone. The serum alkaline phosphatase was elevated to 18 units; the calcium and phosphorus levels were normal. A biopsy was done, and the pathologist's diagnosis was osteolytic osteogenic tumor of bone. Roentgen therapy was given for thirty-one months, with no essential change in the roentgenograms. The patient died of metastasis three and a half years later.

[ED. NOTE.—The very rare location of the lesion in this case, in which a thorough study of the microscopic and roentgenologic findings was made and the end result was obtained, makes reports of this type of value. My statistical studies of tumors of bone have been based on facts obtained from proved microscopic changes, histopathologic determination of the grade of malignancy and subsequent follow-up of cases.

Statistical reports without a report of the microscopic studies are not based on sufficient evidence of proof of malignancy and therefore are of less value in determining the benefits of treatment and prognosis than those based on microscopic studies.]

McNattin,<sup>66</sup> stimulated by the lack of satisfactory opinions concerning any one method of treatment of osteogenic sarcoma, reports a small series of cases in which the patients were treated by roentgen rays for from sixty to one hundred and forty treatments. The treatments were given over multiple portals, and amputation was done when the first signs of irradiation necrosis appeared. He believes that this form of therapy gives the best prognosis and that delay of amputation does not increase the likelihood of distant metastasis. He believes that if serial roentgenograms show some recession of the lesion, indicating radiosensitivity in this type of sarcoma, the total amount of irradiation may be decreased and amputation may be avoided.

[ED. NOTE.—Treatment by means of roentgen rays given preoperatively followed by amputation (Ferguson) delays removal of a malignant lesion. Such a delay is contrary to the common belief that early eradication is the method of choice. Unless there is microscopic proof of the grade of malignancy, I hardly feel that the results of treatment of osteogenic sarcoma by roentgen therapy alone are acceptable.]

Osteochondrosarcoma: Haggart, Hare and Marks<sup>67</sup> present a case in which osteochondrosarcoma arose from the rami of the pubis and ischium. The surgical removal of the tumor was made difficult by its location, since it was adjacent to and compressing the rectum.

Kemper and Bloom<sup>68</sup> present a case of osteochondrosarcoma. The patient was a girl, 13 years of age. Biopsy revealed a spindle cell osteochondrosarcoma of the right tibia without metastasis, and amputation through the lower part of the thigh was done. Two years subsequently there was an osteochondrosarcoma of the femur. At this time a midthigh amputation was done. Then about five months later a maxillary tumor, a mass in the upper right quadrant of the abdomen and recurrence of the osteochondrosar-

66. McNattin, R. F.: Treatment of Osteogenic Sarcoma with Preoperative Roentgen Radiation in Large Doses, *Radiology* 42:246-248 (March) 1944.

67. Haggart, G. F.; Hare, H. F., and Marks, J. H.: Clinico-Pathological Conference [Osteochondrosarcoma], *Radiology* 43:378-382 (Oct.) 1944.

68. Kemper, J. W., and Bloom, H. J.: Metastatic Osteochondroma of Maxilla from Primary Tumor of Tibia: Report of Case, *Am. J. Orthodontics (Oral Surg. Sect.)* 30:704-708 (Nov.) 1944.

64. Gershon-Cohen, J., and Doran, R. E.: Fatigue-Stress Fractures: Diverse Anatomic Location and Similarity to Malignant Lesions, *U. S. Nav. M. Bull.* 43: 674-684 (Oct.) 1944.

65. Friedman, S. T.: Osteogenic Osteolytic Sarcoma of the Os Pubis, *Am. J. Surg.* 64:248-253 (May) 1944.

coma in the femur were found. A biopsy of the mass of the maxillary region was done, and the same pathologic tissue was found, that is, osteochondrosarcoma. This was excised twice by cautery as a palliative measure. Postmortem examination three years or more following the first operation revealed retroperitoneal and sternal metastatic growths but none in the lung.

*H. Metastatic Tumors.*—Fibrosarcoma: Carroll and Martin<sup>69</sup> report on a series of 40 cases of fibrosarcoma of the extremities seen over a period of thirty years and believe that in those of longer duration (an average of ten and a half years) before treatment is started there is better progress than those of short duration. There was a history of trauma in 2 cases. The authors found that local recurrence is characteristic of this lesion unless wide excision or amputation is performed and also that metastasis to regional lymph nodes occurred in 1 out of every 8 cases. In view of this, they believe that excision of the regional nodes should be routine. They feel that irradiation of these tumors has been ineffective in their experience.

[ED. NOTE.—The apparent good results in slow-growing and long-standing tumors of this class are directly dependent on the low grade of malignancy.]

Friedman<sup>70</sup> presents 2 cases and believes that local resection of a connective tissue type of fibrosarcoma is commonly followed by a recurrence. Postoperative roentgen therapy, even in large doses, will prevent only a small part of recurrences. He believes that the postoperative interstitial insertion of radium is the most effective method of destroying tumor cells which may remain in the region of the operation.

Olin<sup>71</sup> reports a case of fibrosarcoma with destruction of the glenoid cavity and apparent involvement of the head of the humerus. A shoulder girdle amputation was performed, and the pathologic examination showed fibrosarcoma. Metastasis to bone and lungs developed subsequently and resulted in death in a few weeks.

Steiner<sup>72</sup> presents an interesting and complete study of an unusual case of widespread multiple fibrosarcoma of bone with visceral lesions involv-

ing the reticuloendothelial system. The lesions arose almost simultaneously throughout the body in the course of a few months. A thorough post-mortem study was made yet no one lesion was deemed primary.

Rhabdomyosarcoma: Garber<sup>73</sup> discusses the rarity of rhabdomyosarcoma and presents a verified case in which the lesion occurred in a man of 68 years. During a course of six months, pain and a progressively enlarging tumor appeared in the left shoulder. The roentgenograms revealed a destructive lesion involving the upper part of the humerus, with characteristics of osteogenic sarcoma. After a course of roentgen therapy, no regression of the lesion occurred and surgical exploration was performed. The patient was apparently well after six months.

Carcinoma: Colonna<sup>74</sup> emphasizes that pain appears early in carcinoma of bone and should not be ignored. He insists on a complete history, a thorough physical examination and laboratory and roentgenographic studies for determination of the diagnosis but feels that even then microscopic study and passage of time may alter an originally correct diagnosis. He further feels that the public should be educated to recognize signs, symptoms and prognosis of carcinoma of bone.

[ED. NOTE.—Roentgenographic examination of painful areas will often permit early recognition of tumors and lead to a true diagnosis and treatment of a malignant lesion of bone. The grade of malignancy, as determined by the microscopic study of the tissue removed, then becomes an important factor in deciding the type of treatment and the prognosis.]

Paletta and Lehman<sup>75</sup> review 267 cases of carcinoma of the breast and make a comparative study of those in which there is metastasis to bone and viscera. They conclude that there is a slightly higher degree of malignancy in cases in which there is metastasis to bone than in cases in which there is metastasis to viscera.

Bertin<sup>76</sup> presents 3 cases in which metastatic lesions of bone were the first symptoms noticed

69. Carroll, G. A., and Martin, T. M.: Fibrosarcoma of the Extremities, *S. Clin. North America* 24:1220-1227 (Oct.) 1944.

70. Friedman, M.: Treatment of Connective Tissue Fibrosarcoma with Surgery and Radium, *Bull. Hosp. Joint Dis.* 4:66-69 (Oct.) 1943.

71. Olin, H. A.: Primary Malignant Neoplasm of the Shoulder Joint, with Report of a Case, *Radiology* 42:359-367 (April) 1944.

72. Steiner, P. E.: Multiple Diffuse Fibrosarcoma of Bone, *Am. J. Path.* 20:877-893 (Sept.) 1944.

73. Garber, R. L.: Rhabdomyosarcoma of the Extremities, *Radiology* 42:595-596 (June) 1944.

74. Colonna, P. C.: Symposium on Early Diagnosis of Cancer: Persistent Bone Pain, *Tr. & Stud., Col. Physicians, Philadelphia* 12:65-66 (June) 1944.

75. Paletta, F. X., and Lehman, E. P.: Carcinoma of the Breast: A Comparative Clinical and Pathologic Study of Tumors Metastasizing to Bone and to Viscera, *Surgery* 15:944-953 (June) 1944.

76. Bertin, E. J.: Metastasis to Bone as First Symptom of Cancer of Gastrointestinal Tract: Report of Three Cases, *Am. J. Roentgenol.* 51:614-622 (May) 1944.

and which later proved to be instances of primary carcinoma of the gastrointestinal tract.

[ED. NOTE.—We have had similar experience in a number of cases. The pathologist usually is able to suggest the probable primary location of the lesion.]

*I. Treatment.*—Phemister<sup>77</sup> discusses ununited fractures and defects of bone and feels that they may be satisfactorily repaired by transplantation of bone. In those instances in which an excision of bone was performed to eradicate a tumor (giant cell sarcoma, large benign tumors of bone, chondrosarcoma and so forth), the defect in the long bones was satisfactorily bridged by transplantation of bone.

[ED. NOTE.—I believe that low grade malignant lesions of bone, if recognized before they reach too great a size, and some benign lesions of bone and cysts of bone may be treated by excision and massive bone grafts with good results.]

*Hormone and Castration Therapy in Carcinoma of Prostate and Breast:* Middleton<sup>78</sup> reports a case of pathologic fracture with delayed union in the subtrochanteric region of the femur which healed after bilateral orchiectomy. The patient died twenty months subsequently, apparently from cerebral vascular accident.

Watkinson, Delory, King and Haddow<sup>79</sup> present 10 cases of carcinoma of the prostate, in 5 of which there was roentgenographic evidence of metastasis to bone. Improvement was noted in 9 cases following therapy with diethylstilbestrol.

Ritvo and Peterson<sup>80</sup> present cases in which the patients had metastasis of bone from carcinoma of the breast and in which regression, noted roentgenographically, was evident after ovarian sterilization. They believe that the regression results from the withdrawal of ovarian hormone. About a third or more of their patients had pronounced relief from pain and general physical improvement, with regression of the lesions of bone noticeable on roentgenographic examination.

[ED. NOTE.—The report of these 3 papers further illustrates the clinical benefits obtained when

patients with metastasis are treated by castration and administration of estrogens (diethylstilbestrol).]

*J. Experimental Studies of Primary and Secondary Tumors of Bone.*—Barrett, Dalton, Edwards and Greenstein<sup>81</sup> report on the history, cytologic and pathologic characteristics and phosphatase activity of a spontaneous, transplantable osteogenic sarcoma carried through eighteen generations of mice (at the time of writing). Early generations of subcutaneous transplants and pulmonary metastasis were osteogenic, with malignant osteoblasts, osteoid tissue and true bone. In later generations the character changed to a more rapidly growing anaplastic tumor which more closely resembled fibrosarcoma, and the capacity of the tumor to cause high alkaline phosphatase activity and to form osteoid tissue was lost or inhibited.

Dunlap, Aub, Evans and Harris<sup>82</sup> review some of the clinical and experimental work on ingestion and implantation of radium and radon in the production of osteogenic sarcoma. Thirteen male rats of the Wistar strain were given radium chloride for twenty days. Eight months subsequently, some objective signs of osteogenic sarcoma began to appear, and eventually osteogenic sarcoma developed in 9 of the 13 rats, with metastasis in 2. All tumor transplants except one failed because rats not of the Wistar strain were used. One transplant grew and since then has been successfully carried in about 50 per cent of attempts through seven serial generations in "Wistar" rats. The transplants have retained their original histologic characteristics and ability to form bone.

Abels and others<sup>83</sup> report that because heptyl-aldehyde bisulfite appeared toxic to human mammary carcinoma in vitro and produced liquefaction necrosis of spontaneous mammary carcinoma in mice they administered it to 14 women who had mammary carcinoma with metastasis to bone; it had no effect of any kind. They conclude that its in vitro effect is due to bisulfite which in vivo was hydrolyzed too rapidly to show any effect.

77. Phemister, D. B.: The Repair of Bone Defects and Ununited Fractures by Bone Transplantation, *Proc. Interst. Postgrad. M. A. North America* (1942), 1943, pp. 105-108.

78. Middleton, A. W.: Union of Pathologic Fracture of Femur Following Castrations for Carcinoma of Prostate, *Am. J. Surg.* 64:144-146 (April) 1944.

79. Watkinson, J. M.; Delory, G. E.; King, E. J., and Haddow, A.: Plasma Acid Phosphatase in Carcinoma of the Prostate and the Effect of Treatment with Stilboestrol, *Brit. M. J.* 2:492-495 (Oct. 14) 1944.

80. Ritvo, M., and Peterson, O. S., Jr.: Regression of Bone Metastases from Breast Cancer After Ovarian Sterilization, *Am. J. Roentgenol.* 51:220-229 (Feb.) 1944.

81. Barrett, M. K.; Dalton, A. J.; Edwards, J. E., and Greenstein, J. P.: Transplantable Osteogenic Sarcoma Originating in C<sub>3</sub>H Mouse, *J. Nat. Cancer Inst.* 4:389-402 (Feb.) 1944.

82. Dunlap, C. E.; Aub, J. C.; Evans, R. D., and Harris, R. S.: Transplantable Osteogenic Sarcomas Induced in Rats by Feeding Radium, *Am. J. Path.* 20: 1-21 (Jan.) 1944.

83. Abels, J. C.; Treves, N.; Herrmann, J.; Singher, H. O.; Kensler, C. J., and Rhoads, C. P.: The Administration of Heptyl-aldehyde Bisulfite to Patients with Inoperable Mammary Carcinoma Metastatic to Bone, *Cancer Research* 4:438-443 (July) 1944.

Frantz, Ball, Keston and Palmer<sup>84</sup> present an interesting study of the effects of activity of the metastatic portions of carcinoma of the thyroid. Radioactive iodine was administered on the assumption that the tumor cells would take up iodine selectively. The postmortem reports showed that only one metastasis had consistently

84. Frantz, V. K.; Ball, R. P.; Keston, A. S., and Palmer, W. W.: Thyroid Carcinoma with Metastases Studied with Radioactive Iodine, *Ann. Surg.* 119:668-689 (May) 1944.

#### IV. CONDITIONS INVOLVING THE HIP JOINT

PREPARED BY JOHN J. FAHEY, M.D., CHICAGO.

Ghormley<sup>85</sup> presents some novel ideas that should be kept in mind when the hip is examined. He presents clearly the complete range of normal motions, and characteristic motion patterns of important diseases are fully described. The limitation in any one plane depends on the position of the limb in other planes. Normally, there is 90 degrees of flexion, and with the extremity slightly abducted and externally rotated between 0 and 20 degrees this is increased 10 degrees. The maximum of external rotation, 70 degrees, is found when the hip is slightly flexed and moderately abducted. The maximum, 40 degrees, of internal rotation is between 10 and 30 degrees of flexion and 20 degrees adduction. Ghormley uses an arthrometer to measure combined motions accurately. Certain diseases present rather characteristic patterns of motion. [Ed. NOTE (J. J. F.).—Persons interested in the mechanics of the hip should resort to the original article.]

Stuck and Hinchey<sup>86</sup> operated on 28 dogs and transplanted various types of pedicled muscle flaps to the hip in an attempt to establish vascular connections. When the dogs were killed, the abdominal aorta was cannulated, the blood vessels of the distal half of the bodies were flushed with isotonic solution of sodium chloride and injected with radiopaque material and roentgenograms were made. The most reliable observations, however, were those based on the pathologic study of the tissue. Various types of operations were performed. In one series, a flap of the gluteus medius muscle was inserted through a hole in the lateral side of the greater trochanter. The most successful type was that in which the vastus lateralis muscle was sutured into a longitudinal slot on the anterior surface of the neck of the femur. After decalcification and staining with hematoxylin and eosin, vascular fibrous connec-

taken up the iodine. The radioactivity of the iodine was not clinically effective for therapeutic "internal irradiation." Possibly, larger amounts might be effective in the well differentiated tissues.

[ED. NOTE.—Such investigations as were carried out by the authors of these experimental studies are commendable, as it is through such efforts that one can look forward to solving the problem of cure of malignant lesions and prevention of metastasis.]

tive tissue connections showed the establishment of an intimate union between the muscle plant and the adjacent bone. The authors have used this operation in combination with vitallium cup arthroplasty, and a Smith-Peterson nail is inserted in cases of monoarticular hypertrophic arthritis and slipped femoral epiphysis. They feel that less pain is found after arthroplasty and more rapid fusion after nailing for slipped femoral epiphysis. They reserve a final appraisal until more evidence is obtained.

Milch<sup>87</sup> believes that "anteversion of the femoral neck" would be better called "abnormal internal torsion of the femoral shaft." He suggests the term "coxa anteverta" to define the initial stages of adolescent epiphysiolysis. "Coxa anteverta" and "anteversion of the femoral neck" represent diametrically opposite conditions. In one, the head tends to lie behind the frontal plane; in the other, in front of the frontal plane of the femur. One is due to relative external torsion of the femur in respect to the head, the other to a relative internal torsion of the femoral shaft in respect to the neck. External rotation should be prevented in the early phase of coxa anteverta. In the late stages, when osteotomy is indicated, internal rotation of the distal fragment is to be undertaken, in contrast to external rotation, which is indicated for the anteversion of congenital dislocation. For anteversion, osteotomy with external derotation of the distal fragment is effective because it overcomes abnormal internal rotation of the shaft. For coxa anteverta, internal rotation is employed.

Townsend<sup>88</sup> describes the internal architecture of the upper end of the femur. The newly formed trabeculae and trabeculated plates are laid down on mechanical principles to withstand the altere

85. Ghormley, J. W.: Hip Motions, *Am. J. Surg.* 66:24-30 (Oct.) 1944.

86. Stuck, W. G., and Hinchey, J. J.: Experimentally Increased Blood Supply to Head and Neck of Femur, *Surg., Gynec. & Obst.* 78:160-163 (Feb.) 1944.

87. Milch, H.: Coxa Anteverta Versus Anteversion of Femoral Neck, *Bull. Hosp. Joint Dis.* 4:79-85 (Oct.) 1943.

88. Townsend, W.: The Architectural Structure of Upper End of Femur in Various Pathologic Conditions, *J. Path. & Bact.* 56:199-207 (April) 1944.

tresses and strains. In coxa valga, the internal architecture undergoes a devolutionary change as a result of modification of the external form and is similar to that of the almost straight reptilian femur. In osteoarthritis, a new compact articular surface is formed superficial to the original one and supported by new trabeculated elements which continue the radiating lines of the original trabecular pattern. A devolutionary process, both in the external architecture and consequently in the internal architecture, takes place in the stumps of the amputated femurs after loss of the full normal function of weight bearing. In 2 specimens examined after amputation, there was an increase in the neck angle, a decrease in the length of the neck and displacement of the head of the femur laterally, backward and downward. The backward displacement represented a retorsion of the head on the neck and exposed the medial part of the anterior surface of the neck to pressure of the iliofemoral ligament and the anterior margin of the acetabulum, thus producing an extension of the articular surface of the head in this region.

Kleinberg<sup>89</sup> reports a case of aseptic necrosis of the femoral head following a dislocation which he believes was not associated with a tear of the round ligament. Exploration of the hip showed a normal-appearing ligamentum teres, grossly and microscopically. He believes that this case demonstrates that rupture of the ligamentum teres is not a constant occurrence in a traumatic dislocation. The author points out that in most cases in which the femoral head is deliberately dislocated from the acetabulum the round ligament is torn, but not infrequently the head can be removed from the acetabulum without rupturing the round ligament.

Salmore<sup>90</sup> measured the pelvifemoral angle in 100 normal persons and found that the most accurate measurements could be made with the patient in the erect position. This angle was defined by Milch as the backward opening angle formed by the axis of the femoral shaft with Nélaton's line; it is valuable in measuring the degree of hip flexion. It was found to be between 50 and 52 degrees in normal adults and children and 58 degrees in the preambulatory infant.

Wellmerling<sup>91</sup> discusses the management of fractures of the femoral neck in relation to certain anatomic considerations of the upper end of

the femur. There are two distinct systems of trabeculae arranged in curved paths, one beginning on the medial side of the upper femoral shaft and curving upward in a fanlike radiation to the opposite portion of the bone and the other originating in the lateral portion of the upper shaft, arching upward and medially. The result of the dense converging trabeculae is a thickened anterior and medial cortex. The fracture is reduced by overtraction in adduction and fixed in a coxa valga position, thereby interlocking the fragments and restoring the normal length. The author relies on his senses and insertion of a guide wire and cannulated nail, controlled by two plane roentgenography, rather than directing devices. For fixation he uses a 5 inch (12.7 cm.) cannulated, vitallium Smith-Peterson nail. The cortex is entered just posterior to the center of the lateral aspect of the shaft and 2 inches (5 cm.) distal to the distal prominence of the trochanter with a 5/32 inch (0.4 cm.) drill. The nail is driven with a 20 degree forward inclination so that it lies in the anteromedial wall of the neck, where the converging trabeculae are the most supportive. If the nail enters the midportion or anterior to it, the nail will emerge through the anterior portion of the neck. [ED. NOTE.—In cases of oblique neck fractures with a spicule beneath the proximal fragment, abduction is usually necessary to accomplish reduction.]

Siris and Ryan<sup>92</sup> believe that the chances of survival are better in cases of intracapsular fractures of the neck of the femur when reduction is done immediately. The use of two machines has simplified the technic and makes draping easier. They do not permit the patients to turn on the uninjured side, because in a certain number of cases this has caused loosening of the nail.

Miller and Bishop<sup>93</sup> reported the case of a 76 year old patient with a fracture of the femoral neck, who died during manipulation of the hip while he was under cyclopropane anesthesia eighteen days following fracture. Autopsy revealed a pulmonary embolism which came from the femoral vein. The authors suggest that early reduction might reduce the incidence of this complication.

Weinberger<sup>94</sup> describes a method for converting fractures of the femoral neck into a valgus

89. Kleinberg, S.: Aseptic Necrosis of the Head of the Femur Following Dislocation of Hip, *Arch. Surg.* 49:104-108 (Aug.) 1944.

90. Salmore, W.: Pelvifemoral Angle, *J. Bone & Joint Surg.* 26:392-393 (April) 1944.

91. Wellmerling, H. W.: New Therapy of Hip-Nailing: Precision Technique for Intracapsular Fractures, *Indust. Med.* 13:809-817 (Oct.) 1944.

92. Siris, I. E., and Ryan, J. D.: Fractures of the Neck of the Femur: An Analysis of 157 Intracapsular and Extracapsular Fractures, *Surg., Gynec. & Obst.* 78:631-639 (June) 1944.

93. Miller, S., and Bishop, H. F.: Fatal Pulmonary Embolism During Manipulation of Hip Under Anesthesia, *Anesthesiology* 5:300-302 (May) 1944.

94. Weinberger, M.: Modification of Lines of Force in Treating Fractures of Neck, *Rev. brasil. de ortop. e traumatol.* 4:235-240 (Sept.-Dec.) 1943.

type or to a Pauwel first degree fracture. He uses strong traction, so that a diastasis is obtained, and the extremity is then brought into 140 degrees of abduction and the fracture fixed by extra-articular fixation.

Schurch,<sup>95</sup> in an article discussing technic and indications for treating fractures of the femoral neck, recommends two x-ray machines and a special table for performing extra-articular pin fixations. In fractures of the trochanteric region, conservative treatment may be tried if conditions are favorable, but if prolonged immobilization is not desirable extra-articular osteosynthesis is indicated.

Stuck<sup>96</sup> states that intertrochanteric fractures occur in older patients and are followed by a much higher death rate than fractures of the neck. They are produced by more serious injury and as a result are attended with more pain and shock. More than half the cases of trochanteric fractures occur in women. In the fractures of the femoral neck the left hip is more commonly involved, and trochanteric fractures are more common in the right hip. The author found a greater mortality in cases of trochanteric fractures. He has never seen a nonunion of a trochanteric fracture, and none has been described in case reports so far as he knows. The main problem, therefore, is to secure union in normal position without coxa vara, shortening or external rotation. Traction has the disadvantages of holding the patient in the supine position, increasing the incidence of bed sores and hypostatic pneumonia and requiring sedatives which depress the patient. Well leg traction produces much residual stiffness and weakness after the fracture is healed. Modern anesthetics, of less shocking action, have made surgical operations on older patients less hazardous. Stuck recommends internal fixation of these fractures when possible. The nursing care is simpler, position can be changed and hospitalization, pain and use of narcotics reduced. Frequent change of position in bed and freedom of movement of the legs are sufficient to reduce pneumonia. He suggests keeping the patient in bed for eight weeks to avoid circulatory disturbances. Of the 65 cases of intertrochanteric fractures, several methods of treatment were used, the most satisfactory being internal fixation and fusion at the shaft with a nail. Coxa vara developed in only 1 case, and in this case the screws were improperly applied.

95. Schurch, O.: *Technic and Indications and Results for Treatment of the Neck of Femur of Extra-articular Osteosynthesis*, *Helvet. med. acta* 10:449-482 (June) 1943.

96. Stuck, W. G.: *Treatment of Intertrochanteric Fractures of Femur*, *Surgery* 15:275-291 (Feb.) 1944.

[ED. NOTE (L. D. B.).—Nonunion in a true intertrochanteric fracture, if it occurs, is certainly rare. A fracture through the base of the neck may be combined with a true intertrochanteric fracture or may be misdiagnosed as an intertrochanteric fracture. Nonunion in this type of fracture occurs frequently.]

Taylor, Neufeld and Jansen<sup>97</sup> report 159 cases of intertrochanteric fractures treated by open reduction and internal fixation. The nail described by Neufeld consists of one piece, pressed into a V shape with a constant angle of 135 degrees. Two screws attach the plate to the lower end of the shaft. After the femur is exposed laterally, a transverse incision is made along the base of the trochanter near the linea aspera, and the vastus lateralis muscle is pulled forward, to minimize loss of blood. In 102 operative cases the mortality was 21.6 per cent, and in 114 nonoperative cases 25.4 per cent. Some of the patients with more serious fractures were not operated on, and that, of course, increases the mortality in that group. Twenty-five per cent died in the first week and 50 per cent of the remainder during the first month. The operation adds to the comfort of the patients and lessens the nursing care. There was no chronic osteomyelitis or persistent drainage in the patients operated on.

Moore<sup>98</sup> discusses the treatment of fractures at the base of the femoral neck and in the intertrochanteric and subtrochanteric regions, for which prolonged hospitalization and expensive nursing care have been required and which have been accompanied with pressure sores and stiffness of joints. He believes that since the introduction of internal fixation and the blade plate, in 1940, these complications have been reduced. The blade which fixes the head and neck is concave, in order to prevent slipping. In 41 patients treated by this method, he reports no operative deaths or nonunions and only 1 minor cutaneous infection.

[ED. NOTE (L. D. B.).—Note the 21.6 per cent mortality rate in the cases with operations and 25.4 per cent in the cases without operations, as reported by Taylor, Neufeld and Jansen<sup>97</sup>.]

At the St. Louis City Hospital Johnson<sup>99</sup> treated over 50 patients with intertrochanteric fractures with hanging casts. The mortality was reduced from 39.3 per cent to 18 per cent and the

97. Taylor, G. M.; Neufeld, A. J., and Jansen, J.: *Internal Fixation for Intertrochanteric Fractures of Bone & Joint Surg.* 26:767-712 (Oct.) 1944.

98. Moore, A. T.: *Blade-Plate Internal Fixation of Intertrochanteric Fractures*, *J. Bone & Joint Surg.* 26:52-62 (Jan.) 1944.

99. Johnson, M. D.: *The Treatment of Intertrochanteric Fractures of Femur with a Hanging Cast*, *Surg., Gynec. & Obst.* 77:592-606 (Dec.) 1943.

duration of hospitalization was shortened. Since the authors adopted the use of a Steinmann pin through the lower part of the femur and the incorporation of the pin in the cast, as suggested by Key, the complications of pressure sores and foot drop have been eliminated. The cast is now applied with the knee in 30 to 40 degrees flexion, with plaster loops on the anterolateral aspect, incorporated at the knee and foot for traction. One to three days later the patient is placed in a wheel chair with a pillow beneath the cast, and the foot-board is turned up, so that the legs hang without support. Crutches may be used in three weeks. The cast is removed after an average of forty-three and four-tenths days and the patient discharged on crutches. Complications, such as pneumonia, decubitus ulcer, stiffness of knees and ankles and weakness from lying in bed are reduced. The reductions have been found to be as good as those obtained with other methods, and nonunion has not occurred. [ED. NOTE (J. J. F.).—This method is novel in the management of these fractures and demands careful consideration. Immobilization with plaster would be expected to cause more articular stiffness than the methods now employed.]

Pascau, Ponce de Leon and Aymerich<sup>100</sup> obtained bony union in 55 of 59 cases of trochanteric fractures treated by traction with a Kirschner wire through the supracondylar portion of the femur. Fifty-one of these patients recovered complete function. Only 2 had a coxa vara deformity. [ED. NOTE (J. J. F.).—The recovery of function of the knee following traction in this age group is usually slow, and not uncommonly some permanent limitation of motion results. The incidence of coxa vara reported in this paper is unusually low, as compared with that in other reports.]

Leadbetter<sup>101</sup> describes an osteotomy high in the cervical axis which is accomplished under full vision and avoids the ascending ramus of the femoral nutrient artery as well as the cervical branches of the circumflex femoral artery. The apposition of abundant cancellous bone is established, with positive pressure beneath the capital portion of the bone in a true valgus position. The osteotomy is made through an anterior approach. The capsule is opened by a cruciate or a semilunar incision, and any comminuted or projecting fragments at the lower part of the head are

removed. The osteotomy is done in the long axis at the junction of its middle and upper thirds, and the neck is then displaced beneath the head to a point within the lower acetabular rim. During the fourth week, the plaster is bivalved and massage and quadriceps-setting exercises begin; the plaster is removed in eight weeks. Eight patients were operated on and observed for at least one year. Every patient had a functioning and weight-bearing hip, and solid union occurred in 6. [ED. NOTE (J. J. F.).—This operation seems promising. Its value will be more accurately determined when more cases are reported. The early quadriceps exercises help to reduce the disability caused by stiffness of the joint.]

Schneider<sup>102</sup> discusses nonunion of the femoral neck and the difficulties encountered with the various present day methods of treatment. He has not found the Blount blade plate fixation for osteotomy, performed for nonunion, to be the entire answer, as in some cases the plate will pull out anteriorly as the extremity goes into external rotation or the screws loosen from the atrophic bone. The Smith-Peterson nail with the Thornton plate has been more satisfactory in his hands, but this method does not always suffice unaided by external support. [ED. NOTE (J. J. F.).—This complication is not as frequent when the plate is introduced in the location used for internal fixation as it is when the plate is introduced high in the trochanteric cancellous bone.]

Rowe and Ghormley<sup>103</sup> state that while most authors believe that bone grafting yields the best end results in the treatment of nonunion of the femoral neck it is well known that only a small percentage of the cases meet the indications for this operation. While many have expressed the opinion that osteotomy offers the simplest and safest procedure for the patient who presents a poor risk and the ones not suitable for osteosynthesis, the authors believe that better mechanical function can be attained by the use of one of the reconstructive operations if the condition of the patient does not prohibit it. If the head is nonviable, the Whitman, the Cplonna or the Albee procedure is indicated. If the head is viable and the degree of absorption rules out a bone-grafting procedure, then the Brackett operation is indicated. A single long vitallium screw, fix-

100. Pascau, I.; Ponce de Leon, A., and Aymerich, E.: *Nonsurgical Therapy of Fractures of the Trochanteric Region*, *Cir. ortop. y traumatol.*, Habana **11**:19-29 (Jan.-June) 1943.

101. Leadbetter, G. W.: *Cervical-Axial Osteotomy of Femur: A Preliminary Report*, *J. Bone & Joint Surg.* **26**:713-720 (Oct.) 1944.

102. Schneider, C. C.: *Sequelae of Fractures of Neck of Femur and Their Treatment*, *Wisconsin M. J.* **43**:799-804 (Aug.) 1944.

103. Rowe, M. L., and Ghormley, R. K.: *Brackett Operation for Ununited Fractures of the Neck of the Femur*, *J. Bone & Joint Surg.* **26**:249-256 (April) 1944.



ing the trochanter and head to the neck, was used in 11 cases in which the Brackett operation was performed, and in 10 results were regarded as good. Ability to walk without support and possession of a practical range of painless motion were obtained in 67.7 per cent of 34 cases. If the articular surface has been destroyed or is ankylosed to the acetabulum, the operation should not be attempted.

McGehee,<sup>104</sup> in discussing the end results of subtrochanteric osteotomy for nonunion of the femoral neck, suggests preliminary traction if the lesser trochanter is above the lower border of the head. The osteotomy is made slightly oblique and at the lower border of the head, just above the lesser trochanter, so that when the medial shift is made the upper portion of the femoral shaft is in direct contact with the greater trochanter and the femoral head. A dead head is not considered a contraindication for operation. Knee hinges with passive motion to 45 degrees were suggested in certain cases to minimize stiffness of the knee. Thirty-eight patients were followed from one to six years postoperatively, and 65 per cent could walk without support and had a good range of motion with little or no pain.

Merle d'Aubigné<sup>105</sup> is of the opinion that it may be possible after several months to accomplish reduction in some cases of intracapsular fractures of the neck of the femur and to repair them with fixation by extra-articular nailing. For fractures that are not reducible, osteotomy has given satisfactory results.

Speed and McGehee<sup>106</sup> report on 52 cases of nonunion of fractures of the neck of the femur treated by subtrochanteric osteotomy and give the final results in 38 cases. The advantages are simplicity and absence of shock in the aged. It may be done for nonunion of long standing and in the presence of a dead head. A cast reaching to the knee, passive motion to 45 degrees as soon as postoperative tenderness subsides and physical therapy are of value in reducing stiffness of the knee in some cases. There were 89.46 per cent favorable results.

104. McGehee, F. O.: Subtrochanteric Osteotomy for Non-Union Fractures of Neck of Femur: A Report of Fifty-Two Cases with End Results of Thirty-Eight. *M. Rec. & Ann.* 38:809-813 (June) 1944.

105. Merle d'Aubigné, R.: Therapy of Old Fractures of Neck of Femur and Pseudarthrosis. *J. de chir.* 58:81-97, 1941-1942.

106. Speed, J. S., and McGehee, F. O.: Subtrochanteric Osteotomy for Non-Union of the Neck of Femur: A Report on Fifty-Two Cases with Final Result in Thirty-Eight. *Cir. ortop. y traumatol., Habana* 11:47-56 (July-Dec.) 1943.

Ossman and Brooke<sup>107</sup> review the literature on the various types of operations devised for the treatment of nonunion of the femoral neck with bone graft and internal fixation. They reported 2 cases with successful results, using a Smith-Peterson nail with a fibular graft. If necessary, preliminary skeletal traction is used. A viable head with minimal absorption of the neck should be a prerequisite.

Harmon and Adams<sup>108</sup> have analyzed the end results in 132 cases of pyogenic coxitis, in order to determine the factors that would lead to the best functional results. They found a relatively benign course in extremely young persons, in older persons, in whom the involvement of bone was restricted, in persons of other age groups in which the bone lesion was small and prolonged traction. The greatest disability occurred in cases of pyogenic coxitis following extensive osteomyelitis. The end result, a stable, painless, movable hip, is more desirable than an ankylosed hip, for it may function for many years before pain occurs. Even when epiphysiolysis and loss of portions of the head and neck occurred, extension was often followed by a favorable outcome. Early diagnosis by aspiration of joint fluid is recommended. Chemotherapy is started immediately after the diagnosis.

Ghormley<sup>109</sup> emphasizes the importance of proper management of several conditions that eventually result in hypertrophic arthritis of the hip. Patients with suppurative arthritis will have a more favorable outcome following the administration of chemotherapy. Slipping of the capital femoral epiphysis should be diagnosed and treated in the preslipping stage. Open reduction of congenital dislocations of the hip, shelving operation for congenital aplasia, perfect reduction of hip in fractures of the acetabulum and guaranteeing weight bearing will reduce the incidence of hypertrophic arthritis. The treatment depends on patency, age and general health. Reduction in weight in obese persons should be considered. Patients are taught to minimize strain and prevent symptoms by the use of heat, crutches. Arthrodesis relieves pain, but

107. Ossman, L. N., and Brooke, W. S.: Smith-Peterson Nail and Fibular Bone Graft in Treatment of Fractures of the Neck of Femur. *Report M. J.* 41:814-818 (Nov.) 1944.

108. Harmon, P. H., and Adams, C. C.: Coxitis: End Results and Considerations and Treatment. *Surg., Gynec. & Obs.* (April) 1944.

109. Ghormley, R. K.: Etiology and Treatment of Hypertrophic Arthritis of Hip. *Staff Meet., Mayo Clin.* 19:559-569 (N)

are not usually willing to accept it, and it is contraindicated when both hips are involved and when the spine is affected. Cup arthroplasty may offer hope of retaining motion and relieving pain in certain cases.

Bergmann<sup>110</sup> discusses aseptic bone necrosis in lesions of the hip. In fractures of the femoral neck, the arteries running along the inner lining of the capsule and entering the head are destroyed, leaving only the vessels of the round ligament, which are insufficient in most instances to keep the head from undergoing necrosis. The adjacent living bone of the distal fragment unites with the head before it has gone through all the stages of reorganization. The endosteum of the distal fragment is the only source from which new bone is laid down, and this is inferior to periosteal callus. The pathologic changes of Perthes' disease (osteochondrosis of the capital epiphysis of the femur), congenital dislocation of the hip and caisson disease are discussed and illustrated with roentgenograms and photographs. [ED. NOTE (J. J. F.).—One interested in the pathologic changes of aseptic necrosis of the head of the femur should read this well illustrated article. In fractures of the femoral neck, there often remains a significant blood supply from the posterior capsular vessels.]

Stephens<sup>111</sup> reviews the literature on iliopectineal bursa and adds 2 cases to the literature. The globular mass may be confused with an enlarged inguinal node or a femoral hernia. Aspiration of seromucous fluid will differentiate it from the former, and pulsation on top of the tumor will distinguish it from the latter. A psoas abscess is more fluctuant. Unilateral chronic disease of the hip joint on the involved side suggests a possible associated bursitis. The simplest method of treatment is aspiration followed by administration of sclerosing solutions. If suppuration occurs, incision and packing are advocated.

Pusitz<sup>112</sup> believes that serious gunshot wounds of the hip and buttock with much fragmentation of the head, seen late, are best treated by resection of the femoral head, sulfonamide compounds and Orr's treatment. A reconstruction or arthrodesis may be performed subsequent to the control of the infection. In cases in which there is much destruction of tissue and in which a portion of

the sciatic nerve is lost, débridement removal of bone and, later, disarticulation of the hip may be indicated. One such case is reported in detail.

Watson and Berkman<sup>113</sup> state that failure to recognize march fractures of the femoral neck promptly may result in serious disability and deformity. They report the case of a soldier 34 years old who experienced sudden severe pain in his hip while hiking and a few days later had pain on the inner side of his thigh and knee. He continued activity, and one month later roentgenograms showed an incomplete fracture with shortening and limited motion of the hip. He was treated by traction for two weeks and then used crutches, without weight bearing, for four months.

Harmon and Adams<sup>114</sup> review the end results of surgical reconstruction in 53 patients who previously had had acute pyogenic arthritis. Chronically discharging sinuses responded satisfactorily to treatment in 80 per cent of the cases. Positional correction of an ankylosed hip, ankylosis of a painful hip and certain plastic procedures performed on young persons were found to be more satisfactory than arthroplastic procedures. Excision of the major part of the ilium in certain cases was thought to be of value when this portion of the pelvis was affected. Disarticulation of the hip joint should receive more consideration in the treatment of persistent suppuration of the hip joint in adults in the presence of osteomyelitis in the upper half of the femur. For young persons with unilateral instability of the hip joint the shelf operation is the procedure of choice, while for adults surgical arthrodesis is performed at the level of the acetabulum after the replacement of the dislocated hip. [ED. NOTE (J. J. F.).—This article is well illustrated and many data are tabulated. Interested persons should refer to the original.]

Milch<sup>115</sup> is of the opinion that the angle of abduction is an unsatisfactory guide in performing an upper femoral osteotomy, and the postosteotomy angle is suggested instead. This angle represents the angle of the neck of the osteotomized femur and is measured by the line of the shaft and the line running from the upper end of the osteotomized shaft to the femoral neck.

113. Watson, F. C., and Berkman, E. F.: Fatigue (March) Fractures of Femoral Neck, *J. Bone & Joint Surg.* 26:404-405 (April) 1944.

114. Harmon, P. H., and Adams, C. O.: Pyogenic Coxitis: Indications for Surgical Treatment in Residual and Chronic Stages and End Results of Reconstruction in Fifty-Three Patients, *Surg., Gynec. & Obst.* 78:497-508 (May) 1944.

115. Milch, H.: The Postosteotomy Angle, *J. Bone & Joint Surg.* 26:394-400 (April) 1944.

110. Bergmann, E.: Role of Aseptic Bone Necrosis in Hip Lesions, *Am. J. Surg.* 63:218-235 (Feb.) 1944.

111. Stephens, V. R.: Tumor of Iliopectineal Bursa: Two Cases, *Arch. Surg.* 49:9-11 (July) 1944.

112. Pusitz, M. E., and Taylor, R. M.: Serious Gunshot Wounds of Hip, *J. Kansas M. Soc.* 44:397-400 (Dec.) 1943.

This angle should not be made greater than the angle of inclination of the outer wall of the level pelvis unless limitation of motion is desired. The postosteotomy angle is greater for any given degree of abduction in the bifurcation operation than in any other type, giving limited motion, and is indicated for tuberculosis and coxitis and contraindicated for congenital dislocation of the hip, fractures of the femoral neck, benign arthritides and all conditions in which motion is desired. The postosteotomy angle can be reduced below the critical value of the level pelvic wall by reducing the degree of abduction of the osteotomized fragment or by resecting the medially projecting apex of the postosteotomy angle. The average angle of inclination of the pelvic wall has been found to be between 205 and 210 degrees. The postosteotomy angle must not be increased beyond this measure if the maximum stability without limitation of mobility is desired.

Bickel and Ghormley<sup>116</sup> find that the results of cup arthroplasty have not been uniformly satisfactory, but in patients who are severely disabled because of pain, deformity or limited motion the results are sufficiently encouraging to justify the operation. Vitallium is the best material yet found to use as a mold. The lucite cup has been discarded because it wears and breaks, necessitating removal. Shortening of the femoral head and neck was observed in many cases when roentgenograms were compared with those taken six months later; in some cases it was so extensive as to allow the cup to ride on the base of the neck against the trochanter and shaft, but the results were no worse. The most disappointing results were obtained in patients operated on for aseptic necrosis. They were poor in over one half of the cases. The results for rheumatoid arthritis were better in men and in operations done on one side. The authors do not advocate operation until the sedimentation rate approaches normal. Eighty-eight of 91 patients were followed from eight months to five years. Only a few felt that they were worse than before the operation. [Ed. NOTE (J. J. F.).—The authors have given a thorough appraisal of arthroplasty, and one should read the original article in order to obtain a detailed report.]

Spira<sup>117</sup> reports the case of a boy unable to stand, even when supported, because of post-

poliomyelitis. Contractures were released by surgical operation, and a strip of fascia lata was brought through a hole in the trochanter and through another hole in the superior pubic ramus and attached to itself, with the extremity held in internal rotation so that the hip could be swung in one plane. The author states that the patient was considerably improved.

Kennedy<sup>118</sup> states that traumatic separation of the upper femoral epiphysis is rare. He reviews 20 cases from the literature, and adds 1. The injury occurs during podalic version and breech extraction or breech presentation and extraction. The case reported by the author is the first reported with cephalic presentation and is the only reported case of bilateral injury. Rotary movements combined with traction on the leg usually produce the injury. The clinical signs are swelling, slight shortening, external rotation, limitation of active motion, painful passive motion and sometimes discoloration and crepitation. The roentgenograms show upward and outward displacement of the proximal end of the diaphysis, profuse callus formation, premature ossification of the capital epiphysis and a prominent subperiosteal reaction around the upper end of the shaft. In cases of severe injury a coxa vara may result. Serial roentgenograms were found of great value in the diagnosis and management.

Haines<sup>119</sup> found that fracture of the acetabulum is an uncommon complication of convulsive therapy. He found 3 cases in the literature and added another. The patient was a boy of 17. A loud snap was heard when convulsions began. Roentgenograms showed a thin-walled acetabulum resembling an Otto type of pelvis, with protrusion of the head. The author has found that complications can be reduced to such a negligible degree by restraints that it is not necessary to use curare, as advocated by others.

Hammond<sup>120</sup> believes that posterior dislocation of the hip associated with a fracture of the acetabulum is the result of considerable trauma applied to the anterior aspect of the knee in the direction of the long axis of the femur when the hip and knee are flexed 90 degrees. An accurate reduction is essential, even if it necessitates open reduction, in order to reduce the incidence of traumatic arthritis. If aseptic necrosis occurs,

118. Kennedy, P. C.: Traumatic Separation of Upper Femoral Epiphysis. *Am. J. Roentgenol.* 51:767-719 (June) 1944.

119. Haines, H. H.: An Unusual Complication of Convulsive Therapy. *Psychiatric Quart.* 16:273-277 (April) 1944.

120. Hammond, G.: Posterior Dislocation of Hip Associated with Fracture. *Proc. Roy. Soc. Med.* 37:281 (April) 1944.

116. Bickel, W. H.; Ghormley, R. K.: Coventry, M. B., and Mussey, R. R., Jr.: Cup Arthroplasty. *Proc. Staff Meet., Mayo Clin.* 19:561-568 (Nov.) 1944.

117. Spira, E.: Restoration of Walking Capacity After Paralysis of Trunk and Leg Muscles: An Operation Restricting the Hip Joint to Movements in Two Axes. *Bull. Internat. Coll. Surgeons* 7:59-62 (Jan.-Feb.) 1944.

weight bearing is delayed until the dead bone has been replaced. Vitallium cup arthroplasty may offer favorable results in certain cases complicated by traumatic arthritis and aseptic necrosis. [Ed. Nore (L. D. B.).—This report should be compared with that of Bickel and Ghormley.<sup>110</sup> The most disappointing results were obtained when operation was performed for aseptic necrosis.]

Wolin<sup>121</sup> describes the case of a man with a Charcot joint who was treated for a dislocation of the hip following a fall; shortly after treatment the dislocation recurred. Roentgenograms showed nothing abnormal, except for the dislocation, until one year later, when a fracture with disorganization of the femoral head was found.

121. Wolin, I.: Tabetic Arthropathy of Hip, *Radiology* 42:79-80 (Jan.) 1944.

#### V. CONDITIONS INVOLVING THE FOOT AND ANKLE

EMIL D. W. HAUSER, M.D., CHICAGO, AND ROBERT P. MONTGOMERY, M.D., MILWAUKEE

Dew and Wooten<sup>122</sup> present a series of 58 march fractures of the metatarsal bones involving 55 trainees. The majority of patients failed to disclose any preexisting pathologic condition of the feet. March fractures are attributable to the carrying of heavy full field equipment and marching of distances longer than 6 miles (9.6 km.) on a hard surfaced road. Local treatment of mild fractures consists in the use of an ice bag for seventy-two hours, a whirlpool bag, a daily massage and crutches; moderate weight bearing within pain limit is allowed. Splinting of any form is not advised because of the ensuing stiffness of the foot and the increasing morbidity. The prophylactic measures advanced by the authors have materially lowered the high incidences of march fracture. They recommend gradual lengthening of the march, progressive increase of field equipment and, what is most important, marching on the soft shoulders of the roads or across the fields.

Krause and Thompson<sup>123</sup> report the results of a study of 200 soldiers who sustained 220 march fractures of the metatarsals between May 1941 and August 1943. Special attention is given to possible predisposing factors, and the various theories which have been advanced to explain the pathogenesis of these fractures are discussed. The immediate cause of the fracture is the rhythmically repeated, subthreshold traumas incident to marching, which, acting by summation, reach a point beyond the ability of the bone to bear stress. Fatigue of the calf muscle causes these subthreshold injuries to be accentuated. The clinical observations and roentgenologic appearances are described in detail. Conservative treatment restores these men to duty with a minimum of time lost.

122. Dew, W. A., and Wooten, J. H., Jr.: March Fractures: A Series of Fifty-Eight, *Mil. Surgeon* 95: 356-359 (Nov.) 1944.

123. Krause, G. R., and Thompson, J. R., Jr.: March Fracture: An Analysis of Two Hundred Cases, *Am. J. Roentgenol.* 52:281-290 (Sept.) 1944.

In a study of a series of 82 cases of march fracture, Kernodle and Jacobs<sup>124</sup> felt that physiologic inadequacy of these feet was a factor even in their series, although they could not demonstrate any gross mechanical inadequacy. The fatigue element with loss of elasticity of the foot has been observed repeatedly and would expose the bony elements to more direct strain. The authors mention a suggestion that march fracture is based on the torsion mechanics of the foot and is due to an acute sinking of a previously well formed foot. Under stress, the medial portion of the anterior part of the foot gives way, and weight bearing is shifted to the second and third metatarsals, which become traumatized and may ultimately break down.

The treatment is varied according to the stage of the fracture when seen. If the period is less than two weeks, a short leg cast molded under the metatarsal heads is applied and a walking rubber attached for a period of three to four weeks, followed by physical therapy for a week, and a metatarsal sponge pad is worn in the shoe. If the time is three to five weeks and there is moderate callus formation, simple pads and physical therapy with moderate rest suffice.

Tyner and Hileman<sup>125</sup> studied 166 cases of march fracture, securing accurate information as to the time the fracture occurred after the beginning of the march, the foot involved and the metatarsal involved. The blood chemistry was studied in 12 cases. Three cases are reported in detail. They believe that the most important factor in the production of these fractures is the increased stress on the metatarsal bones, induced by muscular fatigue.

According to Breck and Higinbotham,<sup>126</sup> march fractures are felt to be due to crystalliza-

124. Kernodle, H. B., and Jacobs, J. E.: Metatarsal March Fractures, *South. M. J.* 37:579-582 (Oct.) 1944.

125. Tyner, F. H., and Hileman, W. T.: March Fractures: An Analysis of One Hundred and Sixty-Six Cases, *Am. J. Roentgenol.* 52:165-172 (Aug.) 1944.

(Footnotes continued on next page)

tion of the calcium phosphate in the bone, similar to the process occurring in metals subjected to intermittent stress, and in this condition the result of excessive minute springing or bending from prolonged marching. A simple treatment consisting in the use of crutches for four weeks from the date of fracture is advocated, with complete restriction of weight bearing during that time. Theoretic and practical considerations to support this method of treatment are given. A series of 54 cases is presented, 48 with excellent results, 5 with poor results (in soldiers with previously symptomatic poor feet) and 1 with a questionable result.

In a statistical study of 47 patients, Leavitt and Woodward<sup>127</sup> discovered that many accepted concepts were disproved and that patients had serious disability which tended to be recurrent and prolonged as a result of march fracture. Many were lost to the combat unit permanently. Training is most important. Foot and general conditioning can be obtained as effectively on soft or natural ground as on hard. Combinations of training on hard and on soft surfaces should be arranged to properly adjust these factors. At present the authors believe that early diagnosis and treatment by absolute freedom from weight bearing until soreness disappears may give the best results. The end results reported in this study have been poor. The authors conclude that march fracture in soldiers is more serious than other reports have indicated. Most patients returned to light duty with their organizations while wearing unpadded plaster casts. They appeared to do little better than patients with unrecognized or late untreated fracture or the few patients who, though seen early, were untreated by choice. These poor results appeared despite the fact that weight bearing in plaster is one of the accepted forms of treatment.

Eddy's<sup>128</sup> discovery of 3 cases of march fracture among women of a shell-loading plant during an eighteen month period prompted him to bring it to the attention of industrial physicians. In these cases the fractures developed after work involving long hours of walking or standing on concrete floors. Treatment consists in immobilization in a boot cast fitted with a walking

iron. The cast is worn six weeks, and roentgenograms should show firm callus before the patient is allowed to walk on the foot. With a properly fitted cast these employees are able to continue their work. The author points out that the question of compensability arises. In this type of case the problem is extremely difficult, as it does not fulfil the requirements of an accident. In his state, however, the compensation act provides for the payment of compensation in all injuries received by an "employee in performing services arising out of and incidental to his employment." Under this interpretation of the law it has been advised that these cases can be accepted under the compensation act.

From a study of 307 cases of march fracture, Bernstein and Stone<sup>129</sup> concluded that prior to the introduction of "speed hikes" and prolonged marches in the curriculum of basic training, this fracture was a rare entity. Soon after this change in the curriculum occurred, this syndrome was seen. The pathologic condition occurred in soldiers irrespective of age, height, weight and general body build. No usual or unusual deformities of the foot were associated with this condition. One or more of the metatarsal bones may be involved at the same time or at different times during the same training cycle. There is no relation between preinduction occupation and development of a march fracture. Contrary to general opinion, this condition occurs in Negro soldiers, although not nearly so frequently as in the white soldiers. In the authors' opinion, the treatment of a march fracture of the foot by immobilization in a plaster of paris bandage is not indicated. These authors use a steel bar from  $\frac{1}{2}$  to  $\frac{5}{8}$  inch (1.3 to 1.6 cm.) wide,  $\frac{1}{8}$  inch (0.3 cm.) thick and 6 inches (15 cm.) long, countersunk into the sole of the shoe on the under side or non-weight-bearing surface of the sole and held in position by four rivets. The relief obtained by this means is definite and becomes more noticeable after several days, that is, as soon as the patient becomes accustomed to walking with a stiff-soled shoe. In this way the patient may continue the greater part of his basic training with little handicap. Most patients continue with their full training and are rarely hospitalized. Occasionally the patient obtains further relief by having a felt pad placed along the longitudinal arch in order to redistribute the weight. The steel bar is kept in position for approximately four to five weeks, at which time

126. Breck, L. W., and Higinbotham, N. L.: March Fracture: New Concepts of Etiology and Logical Method of Treatment, *Mil. Surgeon* 95:313-315 (Oct.) 1944.

127. Leavitt, D. G., and Woodward, H. W.: March Fracture: A Statistical Study of Forty-Seven Patients, *J. Bone & Joint Surg.* 26:733-742 (Oct.) 1944.

128. Eddy, J. H., Jr.: March Fracture in Industry, *New Orleans M. & S. J.* 97:171-173 (Oct.) 1944.

129. Bernstein, A., and Stone, J. R.: March Fracture: A Report of Three Hundred and Seven Cases and a New Method of Treatment, *J. Bone & Joint Surg.* 26:743-750 (Oct.) 1944.

the fracture has solidly healed. The metal bar can then be removed and used again.

Clement<sup>130</sup> reports a study of 32 cases of march fracture in which the fracture was oblique in all early cases and the second and third metatarsal bones only were involved; these were longer than the first metatarsal bones in all but 2 cases, and the fracture line appeared on the medial surface in 29 cases. The increased length of the second and third metatarsal bones deranges the normal tripod structure of the foot, and march fracture results from stress and strain as a result of leverage on the bones, muscle pull of the lumbricalis and interosseus dorsalis muscles, which become spastic from irritation induced by marching.

Bosshardt<sup>131</sup> states that the high incidence of march fracture in German and Swiss armies is due to rigid cadence of marching. There is a definite difference between the occurrence in these two armies and that in the French army, which has an easy marching rhythm. American soldiers generally have led sedentary lives and have poor muscle tone and are therefore liable to have march fracture. The author believes that the fracture is primary and is related to a preexisting static disturbance of the foot, on which rhythmically repeated subthreshold mechanical insults have been acting. The treatment consists in rest and in physical therapy which incorporates exercises especially for dorsal and plantar flexion at the metatarsophalangeal joints.

Salmon's<sup>132</sup> report is based on 5 cases of march fracture. He relates that the absence of a history of direct trauma is responsible for some missed diagnoses. The characteristic appearances of the bone changes in the roentgenograms are described. Immobilization and rest are the suggested therapeutic measures.

Hullinger and Tyler<sup>133</sup> report 313 cases of march fracture in recruits undergoing training. The series includes a small number of cases of stress fractures in bones other than the metatarsals. It is believed that in 100 additional cases there were early march fractures which were completed by a definite trauma, but these cases have not been included in the series. A

detailed statistical analysis is made of the possible relationship of age, weight and other factors to the causation of the condition. The most interesting conclusion is that there is no predisposition to march fracture by any anatomic defect or variation, either acquired or congenital. The roentgenograms in the present series have been compared with three hundred roentgenograms of feet chosen at random. Measurements were taken of metatarsal length, width and spacing; position and conformity of sesamoid bones; length and width of feet, and general formation of foot. "There was no essential difference in the average of measurements in the two groups."

The general conclusion is that march fractures are brought about by trauma in the form of repeated subthreshold insults to the bone caused by walking. The determining factor is essentially a physiologic weakness secondary to fatigue. The incidence of march fractures is directly related to the severity of the training program. A new training order increasing the load carried by a man and the amount of exercise taken immediately resulted in a sharp increase in the number of patients with march fractures admitted to the hospital. The authors favor treatment by immobilization in a light walking plaster cast. They believe that if the bone is not protected from strain in this way callus will be excessive and recovery delayed. With treatment as outlined, all but 2 of the subjects returned to the full rigorous training program in an average of thirty-three days from the time of diagnosis.

[ED. NOTE.—The incidence of march fracture has increased because of the war so that it dominates the literature on the foot. The various reports seem to be in accord with regard to the history, symptoms and findings. There is some variation with regard to causation, but most authors feel that the change in the bone is a matter of strain and that there is an imbalance between the capacity of the bony structure and the demand made on these structures. The result is a disturbance which leads to the hypertrophic changes and the actual fracture. The treatment varies somewhat, although the consensus seems to be that more protection is needed, particularly in the acute phase. The rehabilitation of the foot to gain maximum capacity, so that the patient can carry out the duties of a soldier as soon as possible, is also stressed. This can be accomplished by means of walking casts or by means of a new device, a longitudinal steel bar in the shoe. This seems to fulfil the prerequisites of protection of the metatarsal bone and early resumption of activity.]

130. Clement, B. L.: March Fracture: A Common Disability of the Foot, *J. Bone & Joint Surg.* 26:148-150 (Jan.) 1944.

131. Bosshardt, C. E.: March Fracture: A Common Disability of the Foot in Military Practice, *Arch. Phys. Therapy* 25:41-44 (Jan.) 1944.

132. Salmon, J. K.: March Fracture, *J. Roy. Nav. M. Serv.* 30:1-5 (Jan.) 1944.

133. Hullinger, C. W., and Tyler, W. L.: March Fracture: Report of Three Hundred and Thirteen Cases *Bull. U. S. Army M. Dept.*, September 1944, no. 80, pp. 72-80.

Hullinger<sup>134</sup> states that at Camp Wheeler 71 cases of proved fracture of the calcaneus bone were observed in 53 patients in less than a year. These fractures resulted from the "toughening up" of the training program. Treatment included rest, avoidance of weight bearing on the heels and physical therapy. Later, felt heel inserts or rubber heel elevations or both were used. After a period of eight to ten weeks the men were able to return to full military duty. No recurrences were observed. [ED. NOTE.—This is an interesting report, particularly in the great number of cases that were observed. We have seen such fractures only rarely; it is possible that they may have been overlooked.]

A case report is presented by Raisman<sup>135</sup> of a spontaneous fracture through the apophysis of the right calcaneus bone which occurred in a middle-aged woman with a previous history of syphilis.

Bingham<sup>136</sup> states that 10 per cent of the soldier patients in a designated army camp who complained of painful feet were found to have Morton's syndrome, which is the result of a developmental shortening or relaxation of the first metatarsal segment of the foot. A compensating insole, consisting of a weight-bearing platform for the first metatarsal bone, permitted 76 out of 100 soldiers to continue full military duty.

According to Ilfeld,<sup>137</sup> the observations in a group of 75 white soldiers who were admitted to the orthopedic service with complaints referable to the feet and subsequently discharged from the service were compared with similar observations obtained on examination of 347 white soldiers who were admitted to the orthopedic service with complaints referable to the feet and subsequently discharged from the service with no subjective symptoms. The majority of the men receiving discharges had a so-called third degree pes planus. Seven men of the normal group also had a third degree pronation. It was suggested, therefore, that pronounced pronation may be present without symptoms. Of the 75 men discharged, 48 gave a history of previously using supports; 46 also had backache,

and 54 had pains in the knees. The treatment for pes planus used consisted of properly fitting shoes with individually fitted leather insoles to which were glued pieces of felt for support under the longitudinal and under the transverse arches and foot hygiene. The felt pads were adjustable.

Harris<sup>138</sup> presents numerous cases of various structural defects in the feet and evaluates them relative to the symptoms of the individual case. The article is in the form of a written report on a clinical presentation of cases.

Morton<sup>139</sup> discusses the biomechanics of the foot and its relation to functional disorders and deformities. He describes the evolutionary development of the foot and then shows the relationship of gravity and normal function of the foot. The structure of the foot is primarily concerned with the reaction toward the force of gravity. The relationship of gravity in standing, as well as in walking, is thoroughly worked out. The importance of the anatomic structures as supportive mechanisms against gravity is studied by means of roentgenograms, as well as by barographs and kinetographs. The instrumental analyses have led Morton to the conclusion that gravity is the only mechanical force capable of producing harmful or destructive disorders and deformities of the feet. Imperfections in the skeleton of the foot are direct and immediate sources of disordered function. Through such imperfections the abnormal dissemination of weight stresses and strains permits gravity to exert injurious effects on the overloaded parts. Correction of pedal disorders and deformities requires a clear knowledge of the normal interaction of the feet with the force of gravity so that logical therapeutic procedures can be arrived at.

What Bettmann<sup>140</sup> terms a functional-anatomic analysis, the regaining and maintenance of the originally predominant grasping function of the human foot, is stressed. It is emphasized that exercises for the foot should not be given without accompanying instructions for correct posture in general. Analysis is based on a supinated position for the os calcis in addition to the exercises for the "arch preserver units" of the foot. An exercise sandal supplied with a "Spitzzy Ball" is utilized for exercises.

134. Hullinger, C. W.: Insufficiency Fracture of the Calcaneus Similar to March Fracture of the Metatarsal, *J. Bone & Joint Surg.* 26:751-757 (Oct.) 1944.

135. Raisman, V.: Spontaneous Fracture of the Calcaneus, *Am. J. Surg.* 65:290-292 (Aug.) 1944.

136. Bingham, R.: Painful Feet: Congenital Insufficiency of the First Metatarsal Segment as a Cause Among Soldiers Recently Inducted into the Army, *J. A. M. A.* 124:283-286 (Jan. 29) 1944.

137. Ilfeld, F. W.: Pes Planus: Military Significance and Treatment with Simple Arch Support, *J. A. M. A.* 124:281-283 (Jan. 29) 1944.

138. Harris, R. I.: Foot Problems in the Army and Out of It, *Bull. Vancouver M. A.* 20:273-276 (July) 1944.

139. Morton, D. J.: Foot Biomechanics: Functional Disorders and Deformities, *M. Physics*, 1944, pp. 457-566.

140. Bettmann, E. H.: The Human Foot: A Study of Its Structure and Function; New Functional Exercises, *Arch. Phys. Therapy* 25:13-26 (Jan.) 1944.

In a report of 200 cases of foot disorders selected at random from the orthopedic clinic, Burnham<sup>141</sup> concluded that it would be better carefully to eliminate men with severe foot disorders at the induction centers because it is difficult under military conditions to treat these disorders so that the men can perform useful service. He believes that an improved orthopedic shoe should be issued to all soldiers who exhibit some foot weakness and that the shoe should protect the trainee against acute foot strain which leads to a pes planus. He also urges conservative measures rather than any radical operation with regard to the treatment in military service.

Hauser<sup>142</sup> states that the cause of most common foot disorders is functional decompensation or an imbalance between the work required of the foot and the capacity of the foot to do the work. Increase in load may cause this; standing on hard surfaces and wearing stiff-shanked shoes or shoes with high, narrow heels are causative factors. If the foot is in valgus position, it should be brought into varus position. Shoe corrections may help; a medical wedge on the heel and a comma-shaped bar higher on the outside, which does not go under the fifth metatarsal bone, to bring the anterior part of the foot into relative pronation, is recommended. In addition, the patient must be taught how to stand and how to walk and given special foot exercises. He must have rest periods which are controlled and functional exercises graded to individual needs.

Cleveland, Willien and Doran<sup>143</sup> have operated on 25 soldiers, including 1 officer and a nurse. In 22 of the cases the patients' subsequent fate is known. Half of the soldiers operated on for a single bunion returned to full duty, but only 13 per cent of those with bilateral bunions returned to full duty after operation. A comparison of different operative procedures led the authors to believe that Keller's operation is the method of choice because of good and quick healing, relatively simple after-treatment and a quicker recovery than after other operations. It is emphasized that in general the results of operations for hallux valgus in soldiers are unsatisfactory and that no operation for bunion should be undertaken, especially for bilateral bunions,

unless there seems to be a reasonable prospect of the soldier's return to full duty.

Silver and Rusbridge<sup>144</sup> state that in view of the relative frequency of sprains of the ankle a method of treatment which returns the soldier to active duty in the shortest time with minimum of disability or hospitalization is greatly to be desired. At a station hospital in North Africa, 74 patients with severely sprained ankles were treated in nine months. Of these, 67 returned to active duty immediately and 2 had associated chip fractures of the lateral malleolus (1 returned to duty immediately and the other was overnight in the hospital because of no transportation). The cases of the 6 remaining patients, who were hospitalized, are analyzed.

The authors advocate a basket weave ankle strapping that does not encircle the leg at any point and that is applied with the foot at right angles to the leg and in neutral position regarding varus and valgus. Strapping the foot in inversion is condemned. Compound tincture of benzoin is applied to the skin prior to the strapping. Immediate use is recommended. They attempted to treat 5 patients with injections of procaine hydrochloride into the tender areas, without strapping. All obtained complete relief at once and walked out unassisted, but all returned the next day limping and with recurrence of disability and pain. They were then treated with a basket weave type of strapping, with good results.

Snow and Kraus<sup>145</sup> describe a method of administering procaine hydrochloride by iontophoresis for painful limitation of motion. The technic consists in the application of a solution of 1 per cent procaine hydrochloride and a 1:20,000 solution of epinephrine in 80 per cent alcohol. A gauze pad two to four layers thick is soaked in the solution and placed over the area to be treated. A crash towel is folded twice, soaked in isotonic solution of sodium chloride and spread over the gauze. A flexible metal electrode which is smaller than the towel is then placed over it. The positive pole of a source of galvanic current is attached to the metal electrode. The electrode is fixed by means of bandages. A neutral electrode of approximately the same size is moistened with weak saline solution and connected to the negative pole. The current is slowly applied and increased to 20 milliamperes and permitted to flow for twenty minutes.

141. Burnham, W. H.: *Army Foot Disabilities*, Mil. Surgeon 95:20-24 (July) 1944.

142. Hauser, E. D. W.: *Common Foot Disorders: Rehabilitation with Physiologic Exercises*, Arch. Phys. Therapy 25:93-95 (Feb.) 1944.

143. Cleveland, M.; Willien, L. J., and Doran, P. C.: *Surgical Treatment for Hallux Valgus in Troops in Training at Fort Jackson During the Year of 1942*, J. Bone & Joint Surg. 26:531-534 (July) 1944.

144. Silver, C. M., and Rusbridge, H. W.: *The Treatment of Sprains of the Ankle*, M. Bull. North African Theat. Op. (no. 5) 1:26-28 (May) 1944.

145. Snow, W. B., and Kraus, H.: *Novocaine Iontophoresis for Painful Limitation of Motion*, Mil. Surgeon 95:360-362 (Nov.) 1944.



The current is gently reduced, and the electrodes are removed. The method of treatment is applicable in all cases in which there is limitation of motion due to muscle spasm. It has the advantage that there is no reaction or danger of infection, as with the injection of procaine hydrochloride.

[ED. NOTE.—The use of local injection is valuable in the treatment of a sprained ankle. It relieves the pain and allows more normal function. It also relieves muscle spasm and permits replacement of the foot into normal position. For minor injuries in which the irritation and spasm are the greatest factors, local injection is often all the treatment that is required. In cases in which there is an extensive tear of the ligament, protection by means of the bandage described is indicated.]

The conditions of acute and recurrent dislocation of the ankle joint, unaccompanied with fracture, do not appear to have achieved due recognition, according to Tucker.<sup>146</sup> His article reports six acute and eight recurrent dislocations of the ankle. The structural factors responsible for the stability of the ankle joint are described. The pathologic conditions of acute and characteristic recurrent dislocation of the ankle joint, the clinical features of dislocation and the method used to demonstrate the lesion are described in considerable accurate detail. Watson-Jones and Pennal recommend local anesthesia. When adequate anesthesia by means of pentothal sodium given intravenously has been obtained, the foot is grasped by one hand and the leg firmly grasped by an assistant. The foot is then forcibly inverted and the contour of the ankle region inspected. If the talus bone is tilted by this maneuver, a crease is evident across the front of the joint. By palpation a gap can be demonstrated antero-laterally between the tibia and the talus bone. Performance of the maneuver under the fluoroscope is recommended if possible, and positive results should be recorded on roentgenograms. Full inversion is all that is needed, and the ease of producing the dislocation is just as significant as the degree of displacement obtained. If the maneuver is performed with care, there is no need to inflict further damage.

The treatment recommended for acute dislocations is immobilization in a skintight plaster extending from the metatarsal heads to the tibial tuberosity. An army boot is fitted over the plaster, and a sponge rubber or felt is placed in the sole of the shoe for resilience. Walking is

encouraged as soon as the pain has disappeared, and the patients soon develop a "heel-toe" type of walking, which is much preferred to the pivoting that occurs with Bohler's walking caliper. The cast is retained for ten weeks, and then normal movements are regained by supervised exercises. The results to date have been uniformly good. A recurrent dislocation of the ankle joint is disabling, and early recognition is urged. Severe sprain should receive appropriate attention in every case, and the manipulation described should be performed to test the integrity of the lateral ligaments. In all cases of acute dislocation, the ankle should be immobilized in plaster for about ten weeks. Injuries of this sort are probably responsible for the lay expression that "sprains of the ankle joint are often worse than a fracture."

[ED. NOTE.—It is difficult to overemphasize the advantages of an examination of an injured ankle with the patient anesthetized or when a local anesthetic is utilized. Even the most skillful clinicians will miss significant pathologic conditions without the use of a general or a local anesthetic.]

Roth<sup>147</sup> describes a case of bilateral foot deformity, probably secondary to a congenital lesion of the rubrospinal tract, characterized by recurrent pes cavus, by complicating local infections from previous operative procedure and, later, by the appearance of dorsal exostoses and severe equinus. An anteroposterior tarsal wedge resection was useful in reconstruction of the right foot. The base of the wedge, which lay on the dorsum of the foot, was  $1\frac{1}{2}$  inches (3.8 cm.) wide. The apex lay in the posterior portion of the os calcis. Care was exerted to leave a sufficient thickness of bone under the distal articular surface of the ankle joint, so that its integrity would not be disturbed at operation.

Brown and Brown<sup>148</sup> present a case showing complete dislocation of the os calcis on the talus with 90 degree lateral rotation of the foot, the scaphoid bone being separated anteriorly from the talus. There was no fracture apparent. The dislocation occurred as a result of an external rotation force. Under pentothal sodium anesthesia, gentle manual traction and internal rotation was accompanied with sudden and nearly complete reduction of the dislocation. The slight displacement was corrected by removal of the original cast and recasting the extremity with the

147. Roth, F. B.: Use of Anteroposterior Tarsal Wedge Resection for Unusual Foot Deformity, *Bull. Hosp. Joint Dis.* 5:26-30 (April) 1944.

148. Brown, M. J., and Brown, W. E.: Subastraloid Dislocation, *Am. J. Surg.* 63:276-277 (Feb.) 1944.

146. Tucker, F. R.: The Stability and Instability of the Ankle Joint, *J. Canad. M. Serv.* 1:411-417 (July) 1944.

foot in full dorsiflexion. A cast was worn two weeks, and roentgen ray check-up showed a normal left ankle. On this day the cast was removed and weight bearing allowed. In four days the swelling was no longer present, and good motion of the joint was present without pain or stiffness. The patient was discharged on full duty in approximately four weeks after the injury.

Braun<sup>149</sup> expresses great satisfaction in the results he obtained by conservative therapy for bilateral acquired pes cavus deformities of severe degree in a 24 year old seaman. The treatment consisted in manual stretching of the contractures, restoration of the articular function by manipulation, fulcral felt blockings and strapings, physical therapy and an appliance to establish proper balance of the feet with weight bearing. He states that this case demonstrates what success can be obtained by an intelligent approach to this condition.

Boyd<sup>150</sup> reports 4 additional cases of talonavicular synostosis, the patients being a white girl of 10 years, a white boy of 10 years, the boy's father aged 45 and the boy's grandmother aged 72. The relationships of the last 3 patients suggest a hereditary nature of the condition.

Cohen<sup>151</sup> reports an additional case (20 previous cases have been reported in the literature) of osteochondritis dissecans of the astragalus. An operation two weeks after the trauma afforded an opportunity to note capsular damage (ecchymosis) which may account for this lesion. Necrosis was rapid and probably occurred, immediately after the vascular damage or, at most, within several weeks. A description of the observations at operation for the removal of the osteochondritic body, the microscopic pathologic changes and the differential diagnostic points between an osteochondritic body and a post-traumatic osteochondral fracture are presented.

Croce and Carpenter<sup>152</sup> state that tearing of the plantaris tendon or tennis leg occurs most frequently in middle-aged persons. The syndrome does not cause much disability and has not been widely investigated. The immediate cause of this syndrome and the end result are not definitely known. The authors present a case history which is unusual for three reasons: 1. The cause was direct trauma. 2. The tear

occurred near the origin of the muscle belly. 3. The injury resulted in a degenerative tumor of the muscle. It would seem that the plantaris tendon was torn from its origin along the linea aspera and probably deprived of its blood supply and a degenerative reaction of the belly of the muscle resulted.

Bickel and Moe<sup>153</sup> have described an operative procedure for the relief of paralytic calcaneal deformity of the foot resulting from poliomyelitis in 13 patients. The method consists in translocating the peroneus longus tendon by sliding it intact around the lateral border of the heel into a groove in the midline of the os calcis in an attempt to improve on the results obtained when the peroneal tendon is cut and transplanted into the tendo Achillis. They concluded that the best results were obtained when the operation was done on patients who had slight remaining power in the gastrocnemius muscles and fair or better power in the transposed peroneal muscle. It was their opinion that the results were strikingly better than if the peroneal tendon had been cut and then transplanted into the tendo Achillis.

A case of hereditary malformations of the hands and feet has been traced through four generations by Stiles and Pickard.<sup>154</sup> The defects in the extremities ranged from gross splitting of the hand or the foot to slight abnormalities of the digits. An inspection of the pedigree reveals that the trait may be inherited as a single dominant. Modifying genes, environmental factors or a combination of both may be responsible for the extreme polymorphism of the character.

Experimental fractures in rabbits were treated by Blum<sup>155</sup> with phosphatase and calcium glycerophosphate with and without an anchoring medium (an alginate gel) employed to prevent the too rapid diffusion of the introduced enzyme from the region of the bone gap. Enzyme and substrate were either injected into the gel, which had been pressed into the bone gap, or were injected into the bone gap, in which the gel was subsequently formed in situ. Progress of repair of the bone was followed by roentgenograms and by histologic examination. The treated fractures showed acceleration of repair as compared with untreated controls.

149. Braun, G. S.: Bilateral Pes Cavus: A Case Report, U. S. Nav. M. Bull. 43:346-348 (Aug.) 1944.

150. Boyd, B. H.: Congenital Talonavicular Synostosis, J. Bone & Joint Surg. 26:682-686 (Oct.) 1944.

151. Cohen, H. H.: Osteochondritis Dissecans of the Astragalus, Bull. Hosp. Joint Dis. 4:86-91 (Oct.) 1943.

152. Croce, E. J., and Carpenter, G. K.: Rupture of the Plantaris Muscle, J. Bone & Joint Surg. 26:818-820 (Oct.) 1944.

153. Bickel, W. H., and Moe, J. H.: Translocation of the Peroneus Longus Tendon for Paralytic Calcaneus Deformity of the Foot, Surg., Gynec. & Obst. 78:627-630 (June) 1944.

154. Stiles, K. A., and Pickard, I. S.: Hereditary Malformations of the Hands and Feet, J. Hered. 34:341-344 (Nov.) 1943.

155. Blum, G.: Phosphatase and the Repair of Fractures, Lancet 2:75-78 (July 15) 1944.

sive chilling and ischemia of all the various tissues of the foot or hand. These are successively affected in the inverse order of their biologic fortitude. The complication of duodenitis with duodenal hemorrhage is described. It is suggested that this may be due to the absorption of toxins from the damaged area. The similarity with Curling's duodenal ulcer in burnt patients is noted.

White and Warren,<sup>167</sup> with regard to immersion foot, believe that they have established the fact that there are two definite factors which account for this painful syndrome. In the early phase of inflammation pain is due to anoxia of the injured superficial tissues and nerve endings. Pain of this type can be controlled by cooling the legs, as this lowers cellular metabolism and makes the reduced demand for oxygen commensurate with the limited supply which can be furnished by the thrombosed superficial blood vessels. The second type of pain is characterized by aching and rigidity of the toes and comes on later, after several days have elapsed after a rescue. This may cause prolonged disability.

Edwards, Shapiro and Ruffin<sup>168</sup> state that exposure of the foot for several days to cold, damp weather frequently results in a condition known as trench foot. The outside temperature required to cause trench foot is not so low as that required for frostbite, mainly because of the contact of the extremity with water. There is an anoxia of the tissues and the muscles which

results in damage to nerves. When the feet get warm after exposure, the toes tingle, burn or ache. In this period of too rapid thawing, much damage may be done. The capillary vessels may be injured. The condition is divided into four degrees according to severity: (1) cool and moist, (2) cold and cyanotic, (3) cold and cyanotic with blebs and (4) gangrenous. The treatment consists in washing the feet with soapy water (70 F.) and then exposing them to warm temperature. Absolute rest in bed is advised and then gradual calisthenics followed by rehabilitation exercises. In case of severe damage, injection of procaine hydrochloride into the lumbar sympathetic chain was tried, but with unsuccessful results. Lumbar sympathectomy seemed to be of some use in grade 4, in which gangrene was present. Prophylactic measures, principally keeping the feet dry and general hygienic measures for the foot, are recommended.

Baker and Kuhn<sup>169</sup> conclude that Morton's metatarsalgia syndrome is caused by a tumor in the fourth plantar digital nerve. The cause of this lesion is questionable, but the anatomic relationships of the nerve and the pathologic observations indicate that it is a degenerative fibrosis of the nerve with neuromatous proliferation resulting from, or irritated by, repeated trauma. The characteristic history of the syndrome and the presence of a localized tenderness to deep palpation in the third web space or between the third and fourth metatarsal head on the dorsal surface of the foot make the diagnosis simple. Excision of the tumor relieves the symptoms.

167. White, J. C., and Warren, S.: Causes of Pain in Feet After Prolonged Immersion in Cold Water, *War Med.* 5:6-13 (Jan.) 1944.

168. Edwards, J. C.; Shapiro, M. A., and Ruffin, J. B.: Trench Foot: Report of Three Hundred and Fifty-One Cases, *Bull. U. S. Army M. Dept.*, December 1944, no. 83, pp. 58-66.

169. Baker, L. D., and Kuhn, H. H.: Localized Degenerative Fibrosis with Neuromatous Proliferation of Fourth Plantar Nerve, *South. M. J.* 37:123-127 (March) 1943.

## PANCREATITIS

### AN ANATOMIC STUDY OF THE PANCREATIC AND EXTRAHEPATIC, BILIARY SYSTEMS

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In the majority of diseases of the upper part of the abdomen, the symptoms are sufficiently well defined to permit a definite diagnosis. Probably the most prominent exception in this respect is the pancreas. At the same time, this organ is often involved in pathologic conditions of the surrounding viscera and even in diseases of more remote regions. The problem of pancreatitis is the old problem of abdominal surgery and, since a direct attack on the pancreas is as yet fraught with so much danger, a proper consideration of prepancreatic and peripancreatic disease, together with the etiologic factors as forerunners of acute and of chronic pancreatitis, becomes of vital importance. There is ample evidence<sup>1</sup> to prove that cholecystitis and acute and chronic pancreatitis coexist in a large percentage of cases, but the cause of such coexistence is still obscure.

Where does the provocative agent come from? Among the many explanations of the cause of pancreatitis, the one attributing the condition to a reflux of bile into the pancreatic duct seemed the most plausible to the greatest number of clinicians until Rich and Duff,<sup>2</sup> seeking the cause of acute hemorrhagic pancreatitis in cases in which there was no ampulla of Vater, conclusively demonstrated that in some cases acute hemorrhagic pancreatitis is due to metaplasia of the epithelium of the duct with associated dilatation of the duct and acinar rupture behind the

obstructing metaplasia. And yet a cursory review of the literature on acute pancreatitis is sufficient to impress on one that there is still a striking lack of agreement among investigators concerning the cause. In order to understand the problem, it is necessary to assemble all the information available and then to weigh the interrelations of these facts.

#### HISTORICAL ASPECTS

The earlier anatomists, among them Galen and Vesalius, gave little thought to the pancreas, believing that it acted as a cushion to support and protect the stomach and adjacent structures; and it was not until 1641 that Moritz Hoffmann first discovered the duct of the pancreas while working on a rooster and showed his findings to Wirsung, who one year later dissected the duct in the pancreas of a human body, thus making possible a proper interpretation of its physiology. In a letter to Jean Riolan Jr., professor of anatomy in Paris, Wirsung gave the world the first account of his important discovery. Wirsung had a drainage of the duct reproduced on a copper plate,<sup>3</sup> from which but few copies were struck off. According to Choulant,<sup>4</sup> only two copies are known to be preserved. Schirmer<sup>5</sup> saw one in the University of Strasbourg and had a photolithographic reproduction of it made.

To G. Dominici Santorini<sup>6</sup> belongs the credit for the first description of the accessory pancreatic duct and for the first representation ap-

From the Department of Surgery, Johns Hopkins University School of Medicine and Hospital, and the Department of Surgery, Duke University School of Medicine and Hospital.

1. Edgahl, A.: A Review of One Hundred and Five Reported Cases of Acute Hemorrhagic Pancreatitis, with Special Reference to Etiology, with a Report of Two Cases, *Bull. Johns Hopkins Hosp.* 18:130, 1907. Mayo, W. J.: The Surgical Treatment of Pancreatitis, *Surg., Gynec. & Obst.* 7:607, 1908.

2. Rich, A. R., and Duff, G. L.: Experimental and Pathological Studies on the Pathogenesis of Acute Hemorrhagic Pancreatitis, *Bull. Johns Hopkins Hosp.* 58:137, 1936.

3. Wirsung, G.: *Figura ductus cujusdam cum multiplicibus suis ramulis noviter in pancreate observ.* Padoue, 1642.

4. Choulant, J. B.: *Geschichte und Bibliographie der anatomische Abbildungen*, Leipzig, R. Weigel, 1852.

5. Schirmer, A. M.: *Beitrag zur Geschichte und Anatomie des Pankreas*, Inaug. Dissert., Basel, L. Reinhardt, 1893.

6. Santorini, G. D.: *Anatomici summi septemdecim tabulae*, Parmae, ex regia typog., 1775, p. 150, tabulae XII and XIII.

proximating accuracy of the arrangement of the ducts in the adult human pancreas. He called attention to the existence of the two papillae in the duodenal mucosa and illustrated them in his published work. But it was Bidloo<sup>7</sup> who first noted the papilla common to both the bile and the pancreatic duct. In this connection, also, Regner de Graaf<sup>8</sup> previously had reported that, contrary to what had been the prevailing opinion, the pancreas might present two or even three ducts.

A complete list of the workers on this particular problem in connection with the pancreas is lengthy<sup>9</sup>; it includes such names as Vesling, Bartholinus, Swalve, Blasius, von Muralt, Henle, Sappey, Charpy, Helly, Verneuil, Hamburger, Huschke, Cruveilhier and Christianus Ludovicus Welsch. Now that the identity of the ducts had been established, investigators, such as Albrecht von Haller, Tiedemann and Bécourt, began to report anomalous conditions<sup>10</sup> of these passages. Meckel's was a significant statement<sup>11</sup>

in explanation of the causative factors involved in the production of the numerous anomalous conditions, i. e., that atrophy of the duodenal end of the accessory duct was the developmental rule. In 1846, Claude Bernard<sup>12</sup> again revived interest in the accessory pancreatic duct, but it was not until 1896, when Langerhans<sup>13</sup> published his dissertation describing its minute anatomy, that a proper physiologic interpretation of the pancreas was made possible.

#### EMBRYOLOGY

In order to more clearly understand the arrangement of the ducts and their accessory features in the adult, it is necessary to start at the very beginning, with the embryology of the organ, which has engaged the attention of many workers.<sup>14</sup>

The pancreas arises, as do all the organs of the gastrointestinal tract, as an outpouching or outbudding from the wall of the primitive gut, like a glove finger pushing out from inside the wall. The hollow of this bud, or finger, forms the final duct; the cells at the end grow and develop into the secreting cells of the acini. The pancreas develops from the duodenum at the level of the hepatic diverticulum,<sup>15</sup> from which the cephalic portion of the head and all the neck,

7. Bidloo, G.: *Anatomia humani corporis*, Amstelodami, vid. J. à Someren, 1685.

8. de Graaf, R.: *Tractatus anatomico-medicus de succi pancreatici natura et usu*, Lugd. Bat., ex off. Hackiana, 1671.

9. (a) Veslingius, J.: *Syntagma anatomicum*, Patavii, typ. P. Frambotti, 1647. (b) Bartholinus, T.: *Anatomia*, Dordrecht, J. Soury, 1656; *Anatomy*, London, Nicholas Culpeper and Abdiab Bole, 1668. (c) Swalve, B.: *Pancreas pancrene*, Amstelodami, E. Weyerstraten, 1667. (d) Blasius, G.: *Zootomie seu anatomes variorum animalium pars prima*, Amstelodami, A. Wolfgang, 1677. (e) von Muralt, J.: *Vade mecum anatomicum*, Tiguri, typ. D. Gessneri, 1677. (f) Henle, F. G. J.: *Handbuch der systematischen Anatomie des Menschen*, Braunschweig, F. Vieweg u. Sohn, 1873. (g) Sappey, M. P. C.: *Traité d'anatomie descriptive*, Paris, V.-A. Delahaye & Cie, 1889, vol. 4, p. 272. (h) Charpy, A.: *Variétés et anomalies des canaux pancréatiques*, J. de l'anat. et physiol. **34**:720, 1898. (i) Helly, K. K.: *Beiträge zur Anatomie des Pankreas und seiner Ausführungsgänge*, Arch. f. mikr. Anat. **52**:773, 1898; *Zur Pankreasentwicklung der Säugethiere*, ibid. **57**:271, 1900-1901; *Zur Frage primären Lagebeziehungen bei der Pankreaslagen des Menschen*, ibid. **66**:631, 1904. (j) Hamburger, O.: *Zur Entwicklung der Bauchspeicheldrüse des Menschen*, Anat. Anz. **7**:707, 1892. (k) Huschke, E.: *Traité de splénologie et des organes des sens*, translated from the German by A. J. L. Jourdan, Paris, J.-B. Bailliére, 1845. (l) Cruveilhier, J.: *Traité d'anatomie descriptive*, ed. 4, Paris, P. Asselin, 1861. (m) Welsch, C. L.: *Tabulae anatomicae*, Lipsiae, H. C. Cröker, 1697.

10. (a) Haller, A.: *Elementa physiologiae corporis humani*, Berne, 1764-1766, vols. 6-8. (b) Tiedemann, F.: *Sur les différences que le canal excréteur du pancréas présente dans l'homme et dans les mammifères*, J. compl. du dict. d. sc. méd. **4**:330, 1819. (c) Tiedemann, F., and Gmelin, L.: *Die Verdauung nach Versuchen*, Leipzig, K. Groos, 1826.

11. Meckel, J. F.: *Handbuch der pathologischen Anatomie*, Leipzig, C. H. Reclam, 1812-1816, vol. 3.

12. Bernard, C.: *Mémoire sur le pancréas*, Paris, J.-B. Bailliére, 1856.

13. Langerhans, P.: *Beiträge zur mikroskopischen Anatomie der Bauchspeicheldrüse*, Berlin, G. Lang, 1869.

14. (a) His, W.: *Anatomie menschlicher Embryonen*, Leipzig, F. C. W. Vogel, 1885, vol. 3. (b) Phisalix, C.: *Étude d'un embryon humain de 10 mm.*, Arch. de zool. exper. et gén. **6**:47, 1888. (c) Zimmerman, J.: *Rekonstruktionen eines menschlichen Embryos von 7 mm.*, (suppl.) Anat. Anz. **4**:139, 1889. (d) Felix, W.: *Zur Leber und Pankreasentwicklung*, Arch. f. Anat. u. Entwicklungsgesch., 1892, p. 281. (e) Janösik, J.: *Histologie a mikroskopická anatomie*, v Praze, Bursík & Kohout, 1892; *Le pancréas et la rate*, Bibliog. anat., 1895, p. 68. (f) Jankelowitz, A.: *Ein junger menschlicher Embryo und die Entwicklung des Pankreas bei demselben*, Arch. f. mikr. Anat. **46**:702, 1895; *Zur Entwicklung der Bauchspeicheldrüse*, Inaug. Dissert., Berlin, G. Schade, 1895. (g) Swaen, A.: *Recherches sur le développement du foie, du tube digestif, de l'arrière-cavité du péritoine et du mésentère*, J. de l'anat. et physiol. **32**:1, 1896; **33**:32, 222 and 525, 1897 (pl. I-II, VII and XVI-XVII). (h) Volker, O.: *Ueber die Verlagerung des dorsalen Pankreas beim Menschen*, Arch. f. mikr. Anat. **62**:727, 1903; *Beiträge zur Entwicklung des Pankreas bei den Amnioten*, ibid. **59**:62, 1902. (i) Kollman, J.: *Handatlas der Entwicklungsgeschichte des Menschen*, Jena, G. Fischer, 1897, vol. 2. (j) Ingalls, N. W.: *Beschreibung eines menschlichen Embryos von 4.9 mm.*, Arch. f. mikr. Anat. u. Entwicklungsgesch. **70**:506, 1907.

15. Thyng, F. W.: *Models of the Pancreas in Embryos of the Pig, Rabbit, Cat, and Man*, Am. J. Anat. **7**:489, 1908.

the body and the tail of the pancreas develop. Diverse views are still entertained concerning the duplicity of the ventral anlage, which arises in close proximity to the common duct. Some maintain that the bud is single, while others

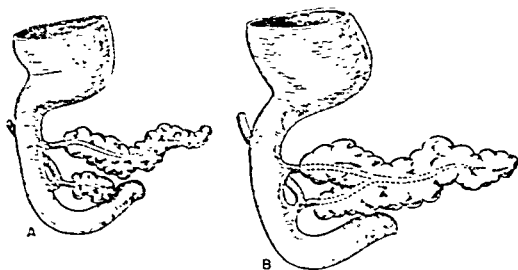


Fig. 1.—Pancreas of a human embryo: *A*, fifth week; *B*, seventh week.

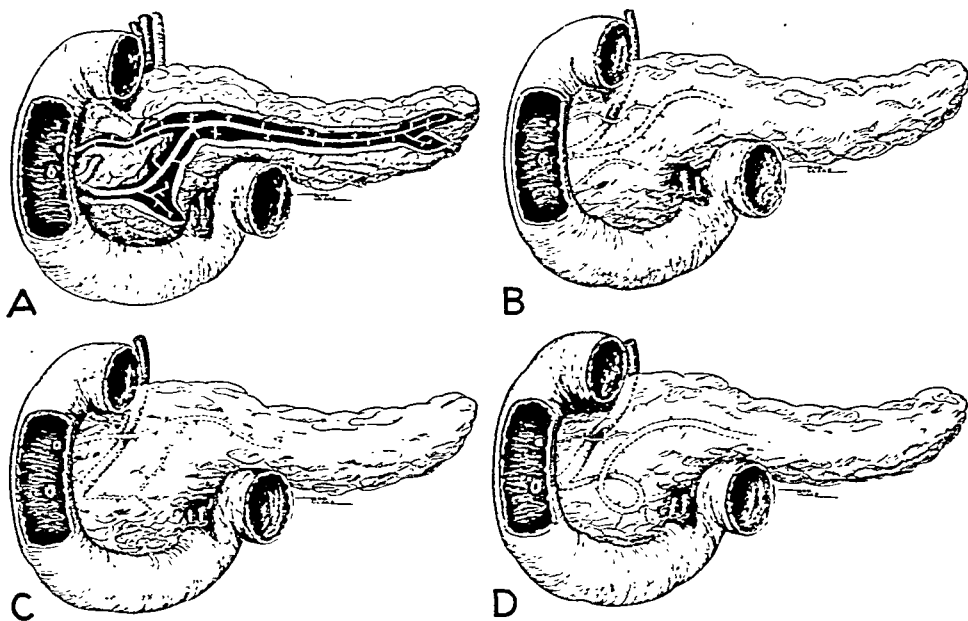


Fig. 2.—*A*, the most constant arrangement of the pancreatic ducts; *B*, specimen with three papillae; *C*, dissected specimen of an adult pancreas showing an embryonic type of duct system in which the accessory duct carries most of the pancreatic secretion; *D*, dissected specimen of an adult pancreas showing an unusual loop configuration of the main pancreatic duct.

old that at the beginning it consists of two lateral halves which subsequently fuse or one of which disappears, perhaps forming the source of aberrant pancreatic tissue often found along the wall of the gut. As development progresses, the ducts unite, as shown in figure 1 *B*, the duct of the dorsal anlage undergoing a certain degree of atrophy at its duodenal end<sup>11</sup> to produce the adult arrangement, shown in figure 2 *A*.

The close relationship between this portion of the pancreas and the common duct is thereby explained. Depending on the eccentricities of development, the relationship will vary somewhat: the common duct may be entirely sur-

rounded by pancreatic tissue; pancreatic tissue may occur even in the wall of the duct itself.

This relation of the exact point of origin of the persisting ventral bud to the common duct determines the final relation of the main pancreatic duct to the common duct. If the pancreatic anlage has grown out from the wall of the common duct itself, the final pancreatic duct will open into the ampulla of the common duct. If the pancreatic anlage has grown out from the wall of the common duct itself, the final pancreatic duct will open into the ampulla of the common duct. If the pancreatic anlage has grown out from the wall of the gut in close proximity to the common duct, the openings of the two ducts will be in close proximity, yet the

pancreatic duct may really open into the intestine and not into the ampulla at all.

The facts seem to be these: Both buds develop by growth in continuity, the dorsal bud giving origin to all of the gland except that portion of the head in close proximity to the common duct and the intestinal wall. The persisting ventral bud grows out but a little way and then fuses with the dorsal bud, giving origin to but a small part of the glandular tissue of the caudal part of the head of the pancreas. In the majority of cases the duct system of this ventral anlage becomes the more important duct system from the point of fusion of the two anlages to the wall of the gut (fig. 1 *B*).

Probably no other region of the body, either in like or in different species, presents more variations than are found in the relation of the component parts of the biliary tract to one another,<sup>16</sup> to the pancreatic duct<sup>17</sup> and to the pancreas and in the relation of all to the duodenum,<sup>18</sup> all of which depend on the relation of the original ventral anlage to the common duct and to the intestinal wall.

#### ETIOLOGY OF PANCREATITIS

The possibility that gallstones lodged in the ampulla of Vater could cause disease of the pancreas by obstructing the main pancreatic duct was first suggested by Lancereaux,<sup>19</sup> who further mentioned that "a gallstone lodged in the common duct at the level of the diverticulum of Vater may occlude the pancreatic duct and produce conditions favorable to the penetration of micro-organisms into the pancreas." It was Körte,<sup>20</sup> when writing on the surgery of the pancreas in 1898, who first noted that diseases of the biliary passages, especially cholelithiasis, are frequently associated with lesions of the pancreas, and he thought that it was probable that inflammation could extend down the bile duct and enter the pancreas. Oser<sup>21</sup> expressed the opinion that catarrhal inflammation might extend from the bile passages to the pancreatic duct, producing obstruction to the pancreatic secretions, with resulting pancreatitis. He further noticed that a calculus lodged in the common duct might partially occlude the adjacent pancreatic duct, producing the same consequences. Ebstein,<sup>22</sup> elaborating still further, stated that a biliary or pancreatic calculus lodged near the orifice of either duct might occlude both, since

the common duct and the pancreatic duct enter the intestine contiguously, at least in some instances.

Since Balser<sup>23</sup> in 1882 first accurately described disseminated fat necrosis, the most extensive investigations have been carried out with regard to the cause of pancreatitis. Thus far four main possibilities have been evolved: 1. A calculus may block the duodenal orifice of the ampulla, so that the common bile and pancreatic duct form a communicating system, allowing bile to flow up the pancreatic duct and infiltrate the pancreas. 2. The sphincter at the duodenal end may become spastic and produce the same condition. 3. The pancreas may be infected by bacteria reaching it by way of the lymph channels from a diseased gallbladder or from a more distant focus of infection by way of the blood stream. 4. Lastly, any obstruction of the pancreatic duct which is complete enough to cause sufficient back pressure of the pancreatic secretions may result in dilatation of the ducts and rupture of the acini, thereby releasing the pancreatic ferments with resulting hemorrhage, fat necrosis and so forth, whether the obstructing factor be metaplasia of the epithelium of the pancreatic duct or its branches, a pancreatic calculus pressing on the pancreatic duct from the adjacent common duct, a calculus impacted at the ampulla or, finally, a carcinoma involving the head of the pancreas.

The theory which possibly boasts the greatest number of adherents depends on the existence of an anatomic arrangement of the duodenal orifices of the common bile duct and the pancreatic duct of such a nature that the impaction of a gallstone in the ampulla of Vater will direct the flow of bile from the bile duct into the pancreatic duct. Since cholecystitis and acute and chronic pancreatitis coexist in a large percentage of cases,<sup>2</sup> the relationship of the common duct to the pancreatic duct has assumed increased importance. The first thing to be determined in the solution of this problem is the approximate percentage of persons in whom the main pancreatic duct and the common bile duct communicate with the duodenum by a common ampulla.

In order to verify the reported discrepancies concerning the relation of the pancreatic duct to the common duct, 250 human specimens were carefully dissected, special attention being paid in each to the terminal ends of the ducts.

The anatomy of the extrahepatic biliary system shows a great variety of arrangement of its

16. Mann, F. C.; Brimhall, S. D., and Foster, J. P.: The Extrahepatic Biliary Tract in Common Domestic and Laboratory Animals, *Anat. Rec.* 18:47, 1920.

17. Mann, F. C.; Foster, J. P., and Brimhall, S. D.: The Relation of the Common Bile Duct to the Pancreatic Duct in Common Domestic and Laboratory Animals, *J. Lab. & Clin. Med.* 5:203 (Jan.) 1920.

18. (a) Letulle, M., and Nattan-Larrier: Région vatrienne du duodénum et ampoule de Vater, *Bull. Soc. anat. de Paris* 12:491, 1898. (b) van Balen Blanken, G. C.: Bijdrage tot de kennis der anatomie van pancreas en lymphaatselsel der primaten, Amsterdam, N. V. Drukkerij "de Nieuwe Tijd," 1912.

19. Lancereaux, E.: *Traité des maladies du foie et du pancréas*, Paris, O. Doin, 1899.

20. Körte, W.: *Die chirurgischen Krankheiten und die Verletzungen des Pankreas*, Stuttgart, F. Enke, 1899.

21. Oser, L.: *Die Erkrankungen des Pankreas*, in Nothnagel, C. W. H.: *Specielle Pathologie und Therapie*, Vienna, A. Hölder, 1898, vol. 17, pt. 2, p. 286.

22. Ebstein, W.: Diabetes Mellitus, Unterleibskolik und Oedeme in ihren Wechselbeziehungen, *Ztschr. f. klin. Med.* 40:191, 1900.

23. Balser, W.: Ueber Fettnekrose, eine zuweilen tödtliche Krankheit des Menschen, *Virchows Arch. f. path. Anat.* 90:520, 1882.

ment parts; in like manner, a comparison relationship between the bile duct and the accessory duct reveals great variability. Furthermore, the method by which the bile duct and accessory ducts enter the duodenum is exceedingly variable, not only in closely related species but in individuals of the same species. Practically all textbooks of anatomy<sup>24</sup> describe these ducts as usually uniting to form a common duct at their duodenal extremities.

#### MATERIAL

The material in this study consisted of both fresh and fixed human pancreases obtained from the autopsy department of pathology and fixed specimens from the department and also from specimens used in the dissecting courses in the department of anatomy at the Hopkins School of Medicine. The pancreases were from 150 men and 100 women ranging in age from 19 to 83 years. Death in no instance was caused by a pathologic process localized in either the duodenum or pancreas.

The entire work on the accessory pancreatic duct was carried out on 100 fresh autopsy specimens, because dissection of the duct after fixation was often difficult and sometimes the patency of the duct could not be accurately determined. The work on the main pancreatic duct and the common bile duct was carried out on 250 specimens, 100 of which were fresh and the remainder which were fixed, because of the difficulty encountered in preserving the delicate membranous septum which often separates the duct of Wirsung from the common bile duct.<sup>25</sup>

#### METHODS

The main pancreatic duct was first located by gross dissection in the middle of the neck of the gland, where pancreatic tissue overlies the superior mesenteric vessels. Here the duct comes within 2 to 3 mm. of the surface and can readily be followed in either direction. The accessory duct was most quickly found by following the main pancreatic duct along its ventral surface toward the duodenum. In these anomalous instances in which the duct could not be found by this method or in which there was no apparent communication between the ducts, the second part of the duodenum was opened along its right free border and the position of the minor papilla ascertained. Then, this being used as a guide, the accessory duct was sought for in the glandular tissue adjacent to the level of the papilla. In those instances in which no communication between the main and the accessory duct could be demonstrated even after pains-

taking dissection, the patency of the accessory duct and the minor papilla was established by inserting a small needle into the main duct and injecting air under minimal pressure while the entire specimen was submerged in water. If no bubbles emerged from the minor papilla, a hypodermic needle was inserted into the accessory duct to establish the patency of its duodenal end. Minimal pressure was used in order to avoid bursting of any natural barrier which might have been present at the blind duodenal end of the accessory duct.

If then no communication could be established, the main duct was injected with methylthionine chloride or eosin after the accessory duct had been ligated where the hypodermic needle had been inserted to test the patency of its duodenal end. Regurgitation of the dye evidenced the presence of a communication between the ducts.

The relation of the main pancreatic duct to the terminal part of the common duct was ascertained by incising the common duct near the entrance of the cystic duct and then opening it to its termination. Likewise, the pancreatic duct was followed from its communication with the accessory duct to its duodenal end, to ascertain what part, if any, it played in the formation of an ampulla. Careful measurements of the distance of the opening from the duodenal end of the bile duct were made with caliper points and recorded.

No attention was given to a study of the intestinal valves. The duodenum was opened along its right free border, and the major and minor papillae were identified in all specimens. Locating the major papilla presented no difficulty; the same, however, was not true of the minor papilla. Many times only after the most careful search could the minor papilla be found.

#### THE MAIN PANCREATIC DUCT

The main pancreatic duct begins in the tail of the gland through the convergence of several small duct radicles and pursues a more or less tortuous course through the body of the gland, approximating the dorsal and cephalic portions of the gland. In the head, however, the duct inclines caudally and dorsally, forming a wide arc with its convexity to the right, as it approaches the dorsal surface of the head of the gland. Reaching the level of the terminal part of the common duct, it runs horizontally to join with the caudal aspect of the common bile duct to form the major duodenal papilla.

In the 100 specimens studied for this purpose the tributaries of the main pancreatic duct in the body of the gland were observed to join the duct almost invariably at right angles and also to alternate with tributaries of the opposite side in the level at which they joined the duct (fig. 2A). The same arrangement was also present in the radicles of these tributaries, except in the head of the gland, in which this conformity was frequently departed from, both as to the position of the tributaries and as to their angle of junction. In 61 instances there was found a moderately large unpaired trunk, as shown in figure 2A, which drained the small lobe of

1. Gray, H.: *Anatomy of the Human Body*, edited by W. H. Lewis, ed. 22, Philadelphia, Lea & Febiger, 1918, p. 1191. Morris, H.: *Morris' Human Anatomy*, edited by C. M. Jackson, ed. 9, Philadelphia, P. Blakiston's Son & Co., 1933, p. 1287. Cunningham, D. J.: *Cunningham's Textbook of Anatomy*, edited by A. B. Binson, ed. 5, New York, William Wood & Company, 1933, p. 1194. Piersol, G. M.: *Human Anatomy*, edited by G. C. Huber, ed. 9, Philadelphia, J. B. Lippincott Company, 1930, p. 1737.

25. Abeberry Oneto, A.: *Anatomía del duodeno y pancreas*, *Semana méd.* 27:395, 1920.



pancreatic tissue overlying the mesenteric vessels, described in 1732 by Winslow and later called to attention by Charpy. In 1 instance this trunk was found to communicate directly with the duodenum through a third papilla, draining the lobe of Winslow and the entire caudal part of the head of the gland, as shown in figure 2B.

The main duct was found to drain the entire tail, body and neck and in 61 instances the dorsal half of the head and the caudal part of the ventral half as well, restricting the accessory duct to the draining of only that part of the head in the immediate proximity of the minor papilla. In 7 instances the accessory duct drained the entire cephalic half of the head, and in 4 instances the main duct was restricted to draining the dorsal and the caudal part of the head, the embryonic arrangement of the ducts, as represented in figure 2C.

In 2 instances another rather unusual arrangement of the ducts was found, similar to that in the 3 specimens found by Baldwin<sup>26</sup> and represented in figure 2D. In these instances the main duct formed a complete loop before joining the common duct. The accessory duct occupied its usual position and joined the main duct before the beginning of the loop. In no instance was the main duct duplicated in the body of the pancreas, as described by Bernard,<sup>12</sup> or the spiral disposition of the pancreatic duct, described by Hyrtl<sup>27</sup> in his "Die Corrosions-Anatomie und ihre Ergebnisse."

#### THE ACCESSORY PANCREATIC DUCT

The accessory duct was present in all 100 specimens dissected for this purpose. In only 89 instances could a communication be found between the ducts after air, dyes or both had been injected and followed by minute dissections.

From the figures in table 1, the main and the accessory duct are shown to communicate within the gland in about 85 per cent of the specimens. Invariably the accessory duct lay on a plane ventral to that of the main duct and communicated with it in the head near the neck of the gland. In 51 instances the accessory duct described two curves as it proceeded toward the duodenum. The first, at the duct end, had

its concavity cephalad, while the shorter one, at the duodenal end, had its concavity caudad, as shown in figure 2A. In 6 instances these curvatures were reversed, and in 24 instances the duct formed a wide curve, at times descending caudal to the main duct. In no instance, however, was it ever found wholly caudal to the main duct. In 4 instances the embryonic arrangement of the ducts was found, i. e., the accessory duct was larger than the main duct and drained the entire cephalic half of the head, together with the neck, the body and the tail, while the main duct was limited entirely to the

TABLE 1.—*Interglandular Communication of the Pancreatic Ducts*

	Junction	No Junction
Opie.....	99	10
Duval.....	?	1
Helly.....	45	2
Charpy.....	28	2
Schirmer.....	65	34
Verneuil.....	20	0
Baldwin.....	66	10
Rienhoff and Pickrell.....	89	11
Total.....	406	70
Per cent.....	85	15

caudal part of the head, as shown in figure 2C. Regardless of the curvature followed or the arrangement of the ducts, in 67 instances the accessory duct was restricted to the ventral and cephalic portion of the head. This finding is in accord with those of the work of Charpy<sup>28</sup> and also the later work of Baldwin,<sup>26</sup> who found that the accessory duct was restricted to the cephalic and ventral aspect in 45 of 66 specimens. Opie, however, stated the belief that the accessory duct drained the "anterior and lower part of the head." And it is a curious fact, in spite of the evidence to the contrary, that most textbooks and atlases of anatomy illustrate the caudal part being drained by the accessory duct.

If one excludes the 11 instances in which no communication could be found between the main and the accessory duct and the 4 instances in which the duct system was reversed, the accessory duct being larger than the main duct—in which naturally the accessory duct approached the duodenum with augmenting caliber—there are 73 of 85 specimens, about 86 per cent, in which there was a normal duct arrangement and the duct approached the duodenum with diminishing caliber. These facts are in accord with Meckel's hypothesis<sup>11</sup> that the pancreatic ducts in the fetus are of equal caliber but that as development progresses the accessory duct atrophies somewhat at its duodenal end. This fact was also noted by Bernard<sup>12</sup> and verified by

26. Baldwin, W. M.: The Pancreatic Ducts in Man, Together with a Study of the Microscopical Structure of the Minor Duodenal Papilla, *Anat. Rec.* 5:197, 1911; The Ductus Pancreaticus Accessorius in Man, *ibid.* 1: 66, 1907.

27. Hyrtl, J.: Die Corrosions-Anatomie und ihre Ergebnisse, Vienna, W. Braumüller, 1873; Handbuch der topographischen Anatomie und ihrer praktischen medicinisch-chirurgischen Anwendungen, *ibid.*, 1865.

Schieffer<sup>28</sup> on human fetuses and still later by Baldwin,<sup>29</sup> who made microscopic preparations of the terminal part of the accessory duct and the minor papilla.

The average diameter of the undistended duct in the 85 specimens with a normal duct arrangement at its point of perforation of the duodenal wall was 1.6 mm. The size of the duct, however, was no criterion of its patency, for only 62, about 73 per cent, were found to be patent by use of the injection method, whereby either air or dyes or both were injected under minimal pressure in order to avoid breaking through any natural barrier which might have been present. This gives, then, 23 specimens, about 27 per cent, which did not communicate with the duodenum. This is considerably higher than Helly's 20 per cent<sup>31</sup> and Baldwin's 10 per cent of 50 specimens,<sup>26</sup> in both groups of which the terminal part of the accessory duct was examined microscopically. These results, however, are in accord with those obtained by use of the injection technic (see table 2).

TABLE 2.—Patency of the Accessory Duct

	Injection Method	
	Patent	Closed
Schirmer.....	65	19
Charpy.....	9	21
Ople.....	79	21
Verneuil.....	20	0
Sappey.....	16	1
Rienhoff and Pickrell.....	62	23
Total.....	271	65
Per cent.....	76	24

In the 4 instances in which the duct system was reversed and the 11 instances in which no intraglandular communication of the ducts could be demonstrated, the accessory duct approached the duodenum with increasing caliber and with a patent papilla, leaving 23 per cent of all specimens in which the papilla was closed, regardless of the duct arrangement. Of practical interest, however, is the fact that in 11 per cent the ducts did not communicate and in 23 per cent the papilla was closed, making a total of 34 per cent in which fluid could not pass from the main duct to the duodenum by way of the accessory duct.

Complete absence of the accessory duct seems to be a rare anomaly, since it occurs in less than 1 per cent of specimens examined (table 3). Inversion of the ducts occurs in about 7 per cent (table 4).

28. Schieffer, J.: Du pancreas dans la série animale, Thesis, Montpellier, 1884.

#### RELATION OF THE AMPULLA OF VATER TO PANCREATITIS

Bécourt,<sup>29</sup> Bernard<sup>12</sup> and Laguesse<sup>30</sup> each mentioned 1 specimen in which the main pancreatic duct opened into the duodenum apart from the orifice of the bile duct. Schirmer<sup>5</sup> found 22 specimens, about 47 per cent, among 47 investigated in which a mucosal septum separated the orifice in such a manner that a true ampulla did not exist. Practically all textbooks of anatomy<sup>24</sup> describe the ducts as usually uniting to form a common channel at their duodenal extremities. Sappey<sup>25</sup> stated that this arrangement is the one which is observed in the great

TABLE 3.—The Accessory Duct

	Present	Absent
Schirmer.....	101	3
Charpy.....	29	1
Helly.....	50	0
Verneuil.....	20	0
Santorini.....	?	0
Bernard.....	?	0
Hamburger.....	50+	0
Sappey.....	17	0
Ople.....	100	0
Baldwin.....	76	0
Rienhoff and Pickrell.....	100	0
Total.....	543	4
Per cent.....		0.737

TABLE 4.—Inversion of Ducts

	Specimens Examined	Inversion of Ducts
Schirmer.....	104	4
Charpy.....	30	3
Bernard.....	?	1
Morel and Duval.....	?	1
Ople.....	100	11
Bimar.....	?	1
Moyse.....	?	1
Baldwin.....	76	3
Rienhoff and Pickrell.....	100	4
Total.....	410	29
Per cent.....		6.61

majority of cases. One of few exceptions to this view is found in the frequently cited work of Letulle and Nattan-Larrier,<sup>18a</sup> who found that a common channel occurred in only 8, about 38 per cent, of 21 specimens.

Schirmer<sup>5</sup> mentioned 11 specimens in his series of 47 in which the pancreatic duct opened into the bile duct and 14 specimens in the same series in which the bile duct opened into the pancreatic duct. Verneuil<sup>31</sup> seemed to believe

29. Bécourt, P. J. G.: Recherches sur le pancréas, Strasbourg, F. G. Levraut, 1830.

30. Laguesse, E.: Sur l'existence de nouveaux bourgeons pancréatiques accessoires tardifs, *Compt. rend. Soc. de biol.* 2:602, 1895.

31. Verneuil, A.: Mémoire sur quelques points de l'anatomie du pancréas, *Gaz. méd. de Paris* 6:384 and 398, 1851; reprint ed., Paris, E. Thunot & Cie, 1851.

that usually the pancreatic duct received the bile duct and that, accordingly, the ampulla of the papilla belonged to the pancreatic duct. Apparently Opie<sup>32</sup> was of the same opinion, for he wrote the following comment concerning the examination of his 100 specimens: "The common bile duct always joined the duct of Wirsung."

Occasionally the pancreatic duct is totally absent. Helly,<sup>31</sup> Charpy<sup>31</sup> and Cruveilhier<sup>31</sup> each mentioned 1 such instance, while Schirmer<sup>5</sup> mentioned 4. Baldwin<sup>26</sup> found 1 specimen in which the main duct was occluded at its duodenal end. And occasionally the common bile duct opens into the duodenum in company with the accessory duct. Schirmer<sup>5</sup> mentioned 5 such instances.

Through the pioneer work of Opie<sup>33</sup> and many subsequent investigators, sufficient reliable evidence has been accumulated to warrant one in suspecting that a reflux of bile up the main pancreatic duct or the anatomic condition which would permit the conversion of the bile duct and pancreatic duct into a communicating system after the impaction of a calculus in the terminal part of the common duct or the ampulla of Vater is the cause of acute hemorrhagic pancreatitis in at least some of the reported cases.

Opie,<sup>32</sup> after examining 100 specimens, found an ampulla in each of 38 specimens, whose measurements varied from "less than 1 mm. to 11 mm." In only 30 specimens did this measurement equal or exceed 5 mm. It is a question whether a common channel should be considered present if the system of the two ducts extends within less than 2 mm. of the summit of the papilla.

Opie<sup>34</sup> pointed out that the presence of a common channel does not necessarily mean that the common duct and the pancreatic duct can be converted into a freely communicating system by an impacted biliary calculus. He stated that in order for this to take place "it is necessary that the diverticulum of Vater be capacious, with a length at least greater than the length of its duodenal orifice." And he found that in 21 of his 100 specimens the diameter of the orifice was equal to or greater than the length of the diverticulum. He concluded, therefore, that in these 21 specimens it was impossible that a calculus, if it were assumed to be approximately spherical and lodged in the orifice, could

only partially occlude the cavity. He<sup>35</sup> likewise asserted that ligation of both pancreatic duct would cause hemorrhagic pancreatitis, and he reported a case in which calculi in the common duct near the ampulla caused obstruction, while bile had not entered the main pancreatic duct as the duct was not dilated. He collected report of 7 similar cases from the literature and concluded, "The lodgment of a stone near the orifice of the common bile duct, where it may at the same time compress or occlude the pancreatic duct, is not uncommonly the cause of pancreatic lesions and disseminated fat necrosis." Moynihan<sup>36</sup> expressed the same opinion, for he wrote

The actual size of the diverticulum and of its opening on the surface of the duodenum are of great importance from a surgical standpoint, for if the diameter of the opening, for example, be 3 mm., and a calculus 4 mm. in diameter reaches the ampulla from the common duct it may block the duodenal orifice, being unable to pass and will, therefore, convert the common bile duct and pancreatic duct into a common closed channel.

By carefully measuring the ampulla, Opie was the first to attempt a solution of this question and since then the most extensive investigation have been carried out with regard to the cause of pancreatitis, most of which have been based on Opie's work or methods of investigation.

More recently, Ruge,<sup>37</sup> Baldwin,<sup>26</sup> Belou,<sup>38</sup> Sweet,<sup>39</sup> Judd,<sup>40</sup> Mann and Giordano<sup>41</sup> and Cameron and Noble<sup>42</sup> have investigated this question, mainly from an anatomic point of view while Dragstedt<sup>43</sup> and Rich and Duff<sup>2</sup> have investigated it mainly from the pathogenic aspect. Ruge found a common channel in 32, about 75 per cent, of 43 cadavers examined. Baldwin in a study of the anatomy of the pancreas, found

35. Opie, E. L.: The Relation of Cholelithiasis to Disease of the Pancreas and to Fat Necrosis, *Am. J. M. Sc.* **121**:27, 1901.

36. Moynihan, B. G. A.: Gallstones and Their Surgical Treatment, Philadelphia, W. B. Saunders & Co. 1904, p. 27.

37. Ruge, E.: Beiträge zur chirurgischen Anatomie der grossen Gallenwege, *Arch. f. klin. Chir.* **87**:47, 1908.

38. Belou, P.: Anatomia de los conductos biliares y de la arteria cística, Buenos Aires, Imp. "Oceana," 1915.

39. Sweet, J. E.: Surgery of the Pancreas, *Internat. Clin.* **4**:293, 1915.

40. Judd, E. S.: Relation of the Liver and the Pancreas to Infection of the Gallbladder, *J. A. M. A.* **77**:197 (July 16) 1921.

41. Mann, F. C., and Giordano, A. S.: The Bile Factor in Pancreatitis, *Arch. Surg.* **6**:1 (Jan.) 1923.

42. Cameron, A. L., and Noble, J. F.: Reflux of Bile up the Duct of Wirsung Caused by an Impacted Biliary Calculus, *J. A. M. A.* **82**:1410 (May 3) 1924.

43. Dragstedt, L. R.; Haymond, H. E., and Ellis, J. C.: Pathogenesis of Acute Pancreatitis (Acute Pancreatic Necrosis), *Arch. Surg.* **28**:232 (Feb.) 1934.

32. Opie, E. L.: The Anatomy of the Pancreas, *Bull. Johns Hopkins Hosp.* **14**:230, 1903.

33. Opie, E. L.: The Etiology of Acute Hemorrhagic Pancreatitis, *Bull. Johns Hopkins Hosp.* **12**:182, 1901.

34. Opie, E. L.: Diseases of the Pancreas, ed. 2, Philadelphia, J. B. Lippincott Company, 1910, p. 15.

at in 20 of 90, 22 per cent, specimens, the ampulla of Vater was absent and the ducts separated by a distinct septum. In 13 per cent, the distance from the orifice of the ampulla to the septum was 2 mm., and in 1 specimen the duct of Wirsung was reduced to a fibrous cord. No detailed measurements of the remaining specimens were given, except that the average distance from the apex of the ampulla to the septum was 4.8 mm.

Bélou, while making a special study of the biliary tract, investigated the relation of the duct of Wirsung to the common bile duct in 50 specimens and found that in 54 per cent the two opened into the duodenum, either separately or at the apex of the ampulla of Vater; in 30 per cent the duct of Wirsung opened from 1 to 2 mm. from the apex, while for the remaining 26 per cent measurements were lacking.

In Osler's series<sup>44</sup> of 100 specimens, in only 32 was the diverticulum of Vater of such size that a small calculus might occlude the orifice without completely filling it and obstructing one or both ducts entering it. Judd<sup>40</sup> studied 170 necropsy specimens for the purpose of determining the percentage of instances in which the anatomic arrangement was such that it would be possible to convert the two ducts into one continuous passageway. This was a possibility in only 4.5 per cent. He concluded that only very exceptionally is there an anatomic arrangement whereby the ducts can be converted either by a stone or by the action of a sphincter, into a continuous passageway permitting bile to flow from the common duct into the pancreatic duct.

Mann and Giordano<sup>41</sup> examined formaldehyde-fixed specimens obtained from 200 consecutive autopsies. Their technic consisted in simple dissection and measurement of the diameter of the ampulla and its duodenal orifice. In 90 specimens, 45 per cent, the ducts were contiguous and opened from 1 to 2 mm. from the apex of the papilla. In 28 specimens, 14 per cent, the length of the ampulla was 3 mm., while in only 7 specimens, 3.5 per cent, did it equal or exceed 5 mm. Since the average diameter of the ampulla was 2.5 to 3.5 mm. they reasoned that the common bile duct and the pancreatic duct could be converted into a continuous channel only by a blockage of the exit in the specimens in which the length of the ampulla was greater than the diameter of its duodenal orifice, i. e., in 7 instances, or 3.5 per cent. They called attention to the fact, previously noted, that the dimensions of the ampulla and the ducts entering it are

often such that a calculus which would become impacted would obstruct both ducts and would not convert them into a continuous channel.

Cameron and Noble<sup>42</sup> resorted to another method of investigation, which consisted in artificially impacting a carefully selected biliary calculus in the ampulla of Vater of a necropsy specimen by stripping it down the common duct and then determining whether a reflux occurred by forcing water or bile down the common duct under a pressure of 100 mm. or less and observing whether it escaped by way of the duct of Wirsung. To insure that the calculus was firmly lodged in the ampulla, a pressure of 1,800 mm. of water was brought to bear on the system. Irregular calculi were used most often, and not infrequently a part of the calculus protruded into the duodenum. Casts of these specimens in which a reflux occurred were obtained by pouring Wood's metal at 180 C. into the common duct, which ran up the duct of Wirsung and hardened immediately. When the cast was exposed, the points between which to measure were usually well defined.

After 100 specimens had been examined, an ampulla was found in 74 instances. In 8 of these, the size of the duodenal orifice was so great and the length of the ampulla so short that it was impossible to convert the two ducts into a common system by means of an impacted calculus. In the remaining 66, this was possible. They concluded, therefore, that in 66 per cent of 100 specimens it was anatomically possible for the common duct and the pancreatic duct to be converted into a single communicating system by an impacted biliary calculus. This figure contrasts sharply with Judd's 4.5 per cent in 170 specimens and Mann and Giordano's 3.5 per cent in 200 specimens.

#### STUDIES ON THE AMPULLA OF VATER

The foregoing review affords evidence that a considerable difference exists between the results of various observers. Because a more detailed study of the exact length of the ampulla of Vater is necessary, especially with reference to the percentage frequency of its variations, and in order to verify the reported discrepancies concerning the relation of the main pancreatic duct and the common bile duct, this study was undertaken.

The specimens consisted of 250 adult human pancreases obtained from both men and women ranging in age from 19 years to 83 years. Death in no instance was due to a pathologic process localized either in the pancreas or in the duodenum. Dissection was carried out in the fresh in 100 of the specimens, as previously outlined, and careful measurements were recorded with

44. Osler, W.: *Modern Medicine*, Philadelphia, Lea & Febiger, 1908, vol. 5, p. 637.

caliper points of the distance from the pancreatic duct, the dividing septum, to the apex of the papilla. These specimens were soon fixed in 4 per cent solution of formaldehyde in order to preserve the delicate membranous septum which often separates the duct of Wirsung from the terminal part of the common duct. The shrinkage caused by fixation falls within the limits of error, since sharply defined points between which to measure are not constant. This is particularly true when one is dealing with an obliquely placed, slitlike duodenal orifice in which there is a difference of 1 mm. or more between the short and the long diameter as measured from the margin of the orifice. In these instances, the long diameter was recorded. The average diameter of the papilla in 250 specimens was found to be 3 mm., with limits of 1.5 mm. and 4.5 mm.

These observations are recorded in table 5 and compared with those of Mann and Diordano and

Cameron and Noble. In 73 of 250 specimens, about 29 per cent, there could be found no junction of the pancreatic and the bile duct, each entering the duodenum contiguously or at separate points, as shown in figure 3 A. In 92 specimens, 37 per cent, the two ducts were contiguous, the dividing septum terminating 1 to 2 mm. from the apex, forming a common orifice for the bile and pancreatic duct, as shown in figure 3 B. In this group a true ampulla was not considered present, since it is a question whether a common channel should be considered present in specimens in which the septum of the two ducts extends within 2 mm. of the summit of the papilla. In 81 instances, 32 per cent, the ducts emptied into a common ampulla from

TABLE 5.—Relation of the Main Pancreatic Duct to the Common Bile Duct

Author	Group	Location of Opening of Pancreatic Duct	Specimens		Distance from Apex of Ampulla to Dividing Septum, Mm.													
			Number	Per Cent	3	4	5	6	7	8	9	10	11	12	13	14		
Mann and Giordano	1	Separately into duodenum	62	21	25	5	3	0	1	2	0	1+						
	2	2 mm. from apex of ampulla	50	45														
	3	3 to 10 mm. from apex	40	20														
	4	Duct absent or closed	8	4														
		Total.....	200	100														
Cameron and Noble	1	Separately into duodenum	26	26	..	..	8	12	13	6	2	3	2	1	1			
	2	2 mm. from apex of ampulla	12	12														
	3	5 to 13 mm. from apex	48	45														
	4	No data.....	14	14														
		Total.....	100	100														
Rienhoff and Pickrell	1	Separately into duodenum	73	29	34	17	11	8	3	3	1	0	2	1	0	1		
	2	2 mm. from apex of ampulla	92	37														
	3	3 to 14 mm. from apex	51	32														
	4	Duct absent or closed	4	2														
		Total.....	250	100														

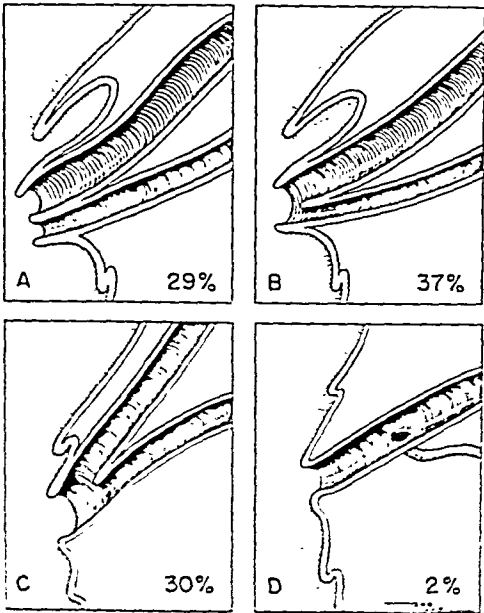


FIG. 3.—Variations of the entrance of the main pancreatic duct into the common duct.

3 to 14 mm. from the apex of the duodenal orifice (fig. 3 C). In 4 of these specimens the length of the diverticulum exceeded 10 mm., as shown in figure 3 D. In 4 instances the pancreatic duct was reduced almost to a fibrous cord and doubtless had little if any function during life, while the accessory duct drained the entire gland.

If one subscribes to the same reasoning as outlined by Opie and employed by Mann and Giordano, the common duct and the pancreatic duct could be converted into a communicating system by a blockage of the exit of the ampulla only in group 3, in which the ducts communicated by a definite diverticulum, and in this group the process could be brought about only in the specimens in which the pancreatic duct empties into the ampulla at a greater distance from the exit than the diameter of the common opening. The average diameter of the ampulla was found to be 3 mm. Of the 32 per cent of the specimens in which an ampulla was present, in 34 specimens, 14 per cent, the opening of the pancreatic duct was 3 mm. from the apex of the papilla.

In the majority of instances, then, a calculus must be 4 mm. in diameter before it can cause obstruction, if one assumes that it is approximately spherical. This, however, seems the exception rather than the rule, since irregularly shaped calculi are encountered more frequently than spherical ones. This leaves, then, 47 specimens, about 18 per cent, in which the length of the ampulla exceeded the average diameter of the duodenal orifice and in which a complete block at the papilla by an impacted calculus would convert the ducts into a communicating system. This reasoning, however, is open to several serious objections. In the first place, conclusions formulated from measurements taken between poorly defined points, of differences of 1 mm. or less, seem decidedly inaccurate, since average measurements may never actually occur in a single instance. In the second place, the obstructing calculus was spherical, when irregularly shaped calculi are encountered more frequently, and, as suggested by Cameron and Noble,<sup>42</sup> a considerable part of an irregularly shaped calculus may project through the orifice of the ampulla into the duodenum, while its length may exceed that of the ampulla, and yet a reflux would be possible. It is true, also, that the greatest diameter of an impacted calculus may equal the long diameter of the ampulla in which it is wholly contained, with a communication existing between the ducts owing to the failure of the irregularly shaped calculus to completely fill the ampulla, which itself may be dilated.

Although it is a matter of definition as to whether an ampulla actually exists in those instances in which the septum extends within 2 mm. of the apex of the papilla, in table 6, in

TABLE 6.—*The Ampulla of Vater*

	Ducts Join to		Specimens
	Form Ampulla	No Junction	Examined
Bécourt.....	?	1	?
Bernard.....	?	1	?
Laguesse.....	?	1	?
Schirmer.....	25	22	47
Letulle.....	8	13	21
Opie.....	89	11	100
Ruge.....	32	11	43
Baldwin.....	26	34	60
Belou.....	8	42	50
Mann and Giordano.....	40	169	209
Cameron and Noble.....	74	26	100
Rienhoff and Pickrell.....	51	169	250
Total.....	413	491	901
Per cent.....	46	53	

which the measurements are given a true ampulla was not considered present in the specimens. From the figures in table 6, we see that

an ampulla is present in about 46 per cent, had the measurements been included in each investigator's report. For example, Cameron and Noble made no mention of the ampullae less than 5 mm., while in Opie's series of 100 specimens, in only 30 did this measurement equal or exceed 5 mm. Oser found only 32 of 100 specimens in which the diverticulum was of such size that a small calculus might occlude the orifice without completely filling it and thus obstruct both ducts. Our findings and the correlation of the greater part of the work done on this particular phase of the problem to the present time lead us to believe that the main pancreatic duct enters the duodenum apart from the common bile duct in 25 to 30 per cent of all cases and that a true ampulla is present in only 30 to 40 per cent.

#### THE RELATION OF THE SPHINCTER OF ODDI TO PANCREATITIS

Although Glisson<sup>45</sup> expressed the opinion that a sphincter existed at the end of the common bile duct, it was first described by Gage,<sup>46</sup> who studied the sphincter in the cat and found sphincters around the pancreatic and common bile ducts and one group of muscle fibers passing around both ducts. Oddi,<sup>47</sup> employing many species of animals, made an extensive comparative anatomic and physiologic study of the sphincter; but, aside from assigning a special sphincter to the duct of Wirsung, he did not study especially the relation of the sphincter of the common bile duct to the pancreatic duct. Somewhat later, Hendrickson<sup>48</sup> studied the sphincter in man, in the dog and in the rabbit. His specimens show muscle fibers surrounding both the common bile and the pancreatic duct.

In the absence of a stone in the ampulla of Vater, it has been suggested that in the instances in which both the bile and pancreatic duct open together in the ampulla, a flow of bile from the common duct might be diverted into the pancreatic duct during life by spasm of the sphincter of Oddi.

The possible importance of the sphincter at the duodenal end of the common bile duct was

45. Glisson, quoted by Oddi.<sup>47a</sup>

46. Gage, S. H.: The Ampulla of Vater and the Pancreatic Ducts in the Domestic Cat, *Am. Quart. Micr. J.* 1:123 and 169, 1878-1879 (pl. xii-xiv).

47. Oddi, R.: (a) D'une disposition à sphincter spéciale de l'ouverture du canal cholédoque, *Arch. ital. de biol.* 8:317, 1887; (b) Sulla tonicità dello sfintere del coledoco, *Arch. per le sc. med.* 12:333, 1888.

48. Hendrickson, W. F.: A Study of the Musculature of the Entire Extrahepatic Biliary System, *Bull. Johns Hopkins Hosp.* 9:221, 1898.

suggested by Archibald.<sup>49</sup> He called attention to the fact that bile might be forced into the pancreatic duct as a result of the spasmodic contraction of the sphincter muscle at the end of the duct. In his interesting experiments testing the resistance of the sphincter in the cat, he introduced into the gallbladder infected bile or bile salts and forced these to enter the pancreatic duct by spasm of the sphincter owing to the sudden rise of pressure in the gallbladder from 200 to 700 mm. of water or to the application of hydrochloric acid to the mucous membrane of the duodenum. Necropsy of the animals that lived several hours revealed acute hemorrhagic pancreatitis and multiple focal liver abscesses.

Knowing that removal of the gallbladder cures most patients with cholecystitis and pancreatitis, Judd<sup>40</sup> studied the changes which result from the loss of this organ and found a dilatation of the common duct with a paralysis of the sphincter. This seemed to explain why removal of the gallbladder relieved the inflammation in the pancreas if it was due to a reflux of bile, the result of a spasmodic contraction of the sphincter; if it was due to an extension of infection from the gallbladder through the lymphatics, then removal of the infected viscus would afford relief.

In order to determine whether it would be possible for the sphincter to convert the common bile duct and pancreatic duct into a continuous channel, Judd examined the sphincter in four species of animals in which the two ducts enter the duodenum together; the dog, the cat, the monkey and man. His examination showed clearly that in almost all instances the muscle fibers are intimately connected with both ducts, so that a contraction of the sphincter would simultaneously close the two ducts and would not convert them into a continuous channel. This was first beautifully shown by Hendrickson<sup>48</sup> with macerated specimens. If Archibald's theory is correct, the sphincter would have to be placed distal to the entrance of both ducts in the ampulla. Mann and Giordano<sup>41</sup> made serial sections of the sphincter in man and found that the usual position of the muscle fibers constituting the sphincter is proximal to the termination of the common duct. These observations show that the usual position and arrangement of the sphincter in man are such that it would not be possible for a contraction of the sphincter

to convert the ducts into a continuous channel, even if they opened into a common ampulla, which in our series was 32 per cent.

Many interesting experiments have shown that the resistance of the sphincter is modified by various conditions: starvation,<sup>50</sup> local irritation of the sphincter<sup>49</sup> and stimulation of the autonomic nervous system. The sphincter is relaxed through the action of the sympathetic system and is thrown into spasm by stimulation of the parasympathetic system. Drugs acting directly on smooth muscle cause spasm increasing the resistance of the sphincter, while drugs which reduce the tonicity of smooth muscle relax the sphincter.<sup>51</sup> The literature is replete with clinical observations regarding the relationship of the sphincter of Oddi to acute pancreatitis,<sup>49</sup> post-cholecystectomy syndrome,<sup>52</sup> dyskinesias of the biliary tract<sup>53</sup> and various forms of jaundice.<sup>54</sup> Recent observations by means of injections of iodized poppyseed oil have clearly demonstrated that spasticity of the sphincter of Oddi occurs in man.<sup>55</sup> Doubilet and Colp<sup>56</sup> measured the resistance of the sphincter in 7 patients with a T tube intubation of the common duct. A variation of 125 to 230 mm. of water, with an average of approximately 165 mm. of water for normal,

50. Cole, W. H.: Relation of Gastric Content to the Physiology of the Common Duct Sphincter, *Am. J. Physiol.* **72**:39, 1925.

51. Brugsch, T., and Horsters, H.: Cholagoga und Cholagogie, *Arch. f. exper. Path. u. Pharmacol.* **118**: 267, 1926. Burget, G. E.: The Relation of the Flow of Bile: II. Effect of Eliminating the Sphincter of Oddi, *Am. J. Physiol.* **79**:130, 1926. Kitakoji, Y.: Studien ueber die Funktionen der Gallenblase und des Oddischen Muskels in Bezug auf die Absonderung der Blasengalle; ueber den Einfluss von Nervengiften auf die Funktionen der Gallenblase und des Oddischen Muskels, *Nagoya J. M. Sc.* **5**:24-29 (Nov. 20) 1930. Nakashima, K.: Studies on the Mode of Bile Outflow: About Oddi's Sphincter, Regulator of Bile Outflow, *Acta scholae med. univ. im Kioto* **9**:357, 1927. Shi, K.: Influence of the Gall Bladder, Oddi's Muscle and the Duodenum upon the Outflow of Bile, *Jap. J. Gastroenterol.* **5**:19, 1933.

52. Rost, F.: Die funktionelle Bedeutung der Gallenblase: Experimentelle und anatomische Untersuchungen nach Cholecystektomie, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **26**:710, 1913. Westphal, K.: Muskelfunktion, Nervensystem, und Pathologie der Gallenwege, *Ztschr. f. klin. Med.* **96**:22, 1923. Footnote 51.

53. Ivy, A. C., and Sandblom, P.: Biliary Dyskinesia, *Ann. Int. Med.* **8**:115, 1934.

54. Manu-Muscel, I., and Pavel, I.: Le spasme du sphincter d'Oddi cause de certains ictères prolongés, *Presse méd.* **38**:1260, 1930.

55. Best, R. R., and Hicken, N. F.: Biliary Dys-synergia: Physiological Obstruction of the Common Bile Duct, *Surg., Gynec. & Obst.* **61**:721, 1935.

56. Doubilet, H., and Colp, R.: Resistance of the Sphincter of Oddi in the Human, *Surg., Gynec. & Obst.* **64**:622, 1937.

49. Archibald, E.: Experimental Production of Pancreatitis in Animals as a Result of Resistance of the Common Duct Sphincter, *Surg., Gynec. & Obst.* **28**:529, 1919. Archibald, E., and Gibbons, E. C.: *Tr. Am. S. A.* **39**:96, 1921.

was found. Duodenal lavage with magnesium sulfate was found to relax the sphincter, while hydrochloric acid caused temporary sphincter spasm, which can be prevented by atropinization. Morphine produces severe spasm lasting as long as four hours, with the pressure reaching 300 mm. of water during the second hour, after 16 mm. have been injected subcutaneously. The action of papaverine and epinephrine was found to be slight.

While there is disagreement as to the frequency with which bile can be held responsible for the development of acute hemorrhagic pancreatitis, all agree that if bile is injected under force into the pancreatic duct experimentally it can produce the condition, as was shown by Opie<sup>33</sup> and since then by many others. The experiments of Flexner<sup>57</sup> and those of other investigators demonstrate that the same result follows the injection of a wide variety of substances, such as oil (Oser,<sup>21</sup> Hess,<sup>58</sup> Guleke,<sup>59</sup> Eppinger<sup>60</sup> and Hewlett<sup>61</sup>), bile (Opie,<sup>33</sup> Flexner,<sup>57</sup> Guleke,<sup>59</sup> Oser<sup>21</sup> and Polya<sup>62</sup>), hydrochloric acid and intestinal secretion (Hlava,<sup>63</sup> Flexner and Pearce,<sup>57</sup> Hildebrand<sup>64</sup> and Rosenbach<sup>65</sup>), intestinal secretion and pancreatic juice, commercial trypsin, calcium and sodium chloride

(Polya<sup>62</sup>), sulfuric acid (Flexner and Pearce<sup>57</sup>), nitric acid (Flexner and Pearce<sup>57</sup>), zinc chloride (Lattes<sup>66</sup>), chromic acid (Lattes<sup>66</sup>), solution of formaldehyde (Flexner and Pearce<sup>57</sup>), calcium chloride (Binet and Brocq<sup>67</sup>) and oleic acid (Hess<sup>58</sup> and Trevor<sup>68</sup>). The same results have been obtained by injecting into the blood vessels substances such as oil, paraffin, wax and lycopodium (Panum,<sup>69</sup> Lépine,<sup>70</sup> Bunge<sup>71</sup> and Guleke<sup>59</sup>). Sailer and Speese<sup>72</sup> suggested that this great variety of substances that cause pancreatic necrosis on injection into the ducts is proof that mechanical distention and injury to the pancreatic tissue are the destructive agents. However, the following substances have been injected into the ducts without harmful effects: blood (Flexner and Pearce<sup>57</sup>) and (Guleke<sup>59</sup>), blood serum (Flexner and Pearce<sup>57</sup>), glycerin (Hess<sup>58</sup>), paraffin (Hess<sup>58</sup>), agar (Lattes<sup>66</sup>) and starch (Hess<sup>58</sup>).

While quantities of 4 to 30 cc. of bile and other fluids were injected forcibly into the pancreatic duct with a syringe, Rich and Duff<sup>2</sup> have shown that injections of smaller quantities of India ink into the pancreatic duct will rupture the smaller ducts and acini even in a large dog, leading to the immediate escape of ink into the interstitial tissues throughout the greater part of the pancreas. Archibald<sup>73</sup> was unable to produce necrosis or hemorrhagic pancreatitis by injecting small amounts (0.75 cc.) of bile into the pancreatic duct. Nordmann,<sup>74</sup> realizing the

57. Flexner, S.: The Constituent of the Bile Causing Pancreatitis and the Effect of the Colloids upon Its Action, *J. Exper. Med.* 8:167, 1906; Experimental Pancreatitis, *Bull. Johns Hopkins Hosp.* 9:743, 1900; On the Occurrence of the Fat-Splitting Ferment in Peritoneal Fat Necroses and the Histology of These Lesions, *J. Exper. Med.* 2:413, 1897. Flexner, S., and Pearce, R. M.: Experimental Pancreatitis, *Univ. Pennsylvania M. Bull.* 14:193, 1901.

58. Hess, O.: Experimenteller Beitrag zur Aetiologie der Pankreas- und Fettgewebsnekrose, *München. med. Wchnschr.* 50:1905, 1903; Experimentelles zur Pankreas- und Fettgewebs-Nekrose, *ibid.* 52:544, 1905.

59. Guleke, N.: Demonstration einer experimentell gewonnenen Pankreasnekrose, *Berl. klin. Wchnschr.* 41:682, 1905; Ueber die experimentelle Pankreasnekrose und die Todesursache bei acuten Pankreaserkrankungen, *Arch. f. klin. Chir.* 75:845, 1905-1906; 85:615, 1908.

60. Eppinger, H.: Zur Pathogenese der Pankreas-fettgewebsnekrose, *Ztschr. f. exper. Path. u. Therap.* 2:216, 1905-1906.

61. Hewlett, A. W.: On the Occurrence of Lipase in the Urine as a Result of Experimental Pancreas Disease, *J. M. Research* 11:1904.

62. Polya, E. H.: Zur Pathogenese der acuten Pankreasblutung und Pankreasnekrose, *Berl. klin. Wchnschr.* 43:1562, 1906; Ueber die Pathogenese der acuten Pankreaserkrankungen, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* 24:1, 1912.

63. Hlava, J.: Some Affections of the Pancreas and Sudden Death from Them, *Sbírka přednášek z oboru lékařsk.*, v Praze, 1899, no. 16, p. 111; Sur la pancréatite hémorragique, *Compt. rend. Cong. internat. de méd.* (1897) (sect. 3) 2:106, 1899.

64. Hildebrand, G.: Zur Pankreaschirurgie, *Arch. f. klin. Chir.* 89:2, 1909.

65. Rosenbach, F.: Gallenstauung im Ductus Wirsungianus durch Stein in der Papilla Vateri als Ursache einer akuten Pankreasnekrose mit galliger Peritonitis, *München. med. Wchnschr.* 65:185, 1918.

66. Lattes, L.: Ueber Pankreasvergiftung, *Virchows Arch. f. path. Anat.* 211:1, 1913.

67. Binet, L., and Brocq, P.: Le rôle du suc intestinal dans la reproduction expérimentale de la pancréatite hémorragique avec stéatonecrose, *Compt. rend. Soc. de biol.* 83:340, 1920.

68. Trevor, R. S.: Some Recent Work on Disease of the Pancreas, *Practitioner* 72:570, 1904.

69. Panum, P. L.: Experimentelle Beiträge zur Lehre von der Embolie, *Virchows Arch. f. path. Anat.* 25:308, 1862.

70. Lépine, R.: Diabète maigre avec intégrité du pancréas, *Lyon méd.* 71:591, 1892.

71. Bunge: Zur Pathogenese und Therapie der acuten Pankreashämorrhagie und abdominalen Fettgewebsnekrose, *Arch. f. klin. Chir.* 71:726, 1903.

72. Sailer, J., and Speese, J.: Acute Pancreatitis, *Tr. A. Am. Physicians* 23:540, 1908.

73. Archibald, E. W., in Lewis, D.: *Practice of Surgery*, Hagerstown, Md., W. F. Prior Company, Inc., 1933, vol. 7, p. 1.

74. Nordmann, O.: Experimente und klinische Betrachtungen über die Zusammengänge zwischen acuter Pankreatitis und Erkrankungen der Gallenblase, *Arch. f. klin. Chir.* 102:66, 1913.



danger of the injection technic, converted the common duct and pancreatic duct into a continuous channel by closing the ampulla of Vater with a purse string suture. Jaundice without hemorrhagic pancreatitis occurred, even though the pancreatic duct was dilated with bile. Mann and Giordano<sup>41</sup> likewise found that if 5 to 10 cc. of bile is forced with a syringe into the pancreatic duct of a dog rupture of the smaller ducts and acini occurs.

Even if the ampulla is obstructed and the ducts converted into a communicating system, will bile flow into the pancreatic duct? Theoretically, it would seem that the direction of flow should depend on the relative pressures developed in the duct system of each gland. Mann and Giordano<sup>41</sup> were unable to inject bile into the pancreatic duct of a dog with the maximal normal secretory pressure of the liver, 350 mm. of bile. The secretory pressure in the pancreatic duct was found to range from 260 to 350 mm. of water. These values are in accord with those of other investigators.<sup>75</sup> It is seen that the maximal secretory pressures of the liver and pancreas are about equal, the former being slightly higher, the difference, however, being possibly great enough to cause bile to flow over into the pancreatic duct. When pressures up to 800 mm. of bile were used, even though the pancreatic duct was filled with bile, acute pancreatitis did not result. Considerable importance has been attached to the observation of Mann and Giordano<sup>41</sup> that during vomiting the pressure in the biliary tract rose to 1,000 mm. of bile, and the suggestion has been made that through such a mechanism vomiting might be thought to cause pancreatic necrosis. It is, however, altogether probable that the general increase in intra-abdominal pressure due to vomiting would affect the two glands alike and no transfer of fluid would occur. Harms<sup>76</sup> reported that during the height of digestion in the unanesthetized dog the secretory pressure of the pancreas is higher than

that of the liver, a finding which would suggest the passage of pancreatic juice into the biliary channels, rather than the reverse.

From these experiments, the conclusion that hepatitis or cirrhosis of the liver is due to passage of pancreatic juice into the bile duct would seem almost as justifiable as that pancreatitis is due to a reflux of bile.<sup>77</sup> Bile may pass into the pancreatic duct for one or all of the following reasons: The secretion of bile is continuous, with changes in rate, while the secretion of the pancreatic juice is intermittent. There are times when the pressure in the pancreatic duct might be considerably less than in the bile duct. The liver has firmer tissue and a stronger capsule than the pancreas. With regard to the volume of fluid secreted, the drainage of the intraductal fluid to the outside of the gland is freer in the pancreas than in the liver. From our study of the pancreatic systems, we found that in 11 per cent the main and accessory ducts did not communicate and in 23 per cent the minor papilla was closed, making a total of 34 per cent in which fluid could not pass from the main duct to the duodenum by way of the accessory duct. These findings are in accord with those of other investigators.<sup>78</sup>

Current theories postulate that bile entering the pancreatic duct in man produces necrosis of the pancreas because of its own irritating and necrotizing properties or its bacterial content or because it activates the inactive trypsinogen of the normal pancreatic secretion while the latter is still in the pancreatic ducts. Persons who emphasize the role of infection introduced by the reflex of bile contend that necrosis of the pancreas is produced either through the direct action of the bacteria or through the destructive effects of trypsin, which follow on the activation of trypsinogen by the bacteria or their products. All authors agree that the peculiar characteristics of the fat necrosis which accompany hemorrhagic pancreatitis depend on the action of pancreatic lipase which is secreted in active form and which escapes into the tissues when necrosis of the pancreas occurs.

The various theories regarding the hemorrhage of acute hemorrhagic pancreatitis are discussed by Gruber.<sup>79</sup> Some authors believe that

77. Diseases of the Liver, Pancreas, and Suprarenal Glands, in Nothnagel, C. W. H.: *Encyclopedia of Practical Medicine*, Philadelphia, W. B. Saunders Company, 1903, p. 642.

78. Schirmer<sup>2</sup> Veslingius and others.<sup>3</sup> Baldwin.<sup>22</sup>

79. Gruber, G. B., in Henke, F., and Lubarsch, O.: *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1929, vol. 5, pt. 2.

75. Herring, P. T., and Simpson, S.: The Pressure of Bile Secretion and the Mechanism of Bile Absorption in Obstruction of the Bile Duct, *Proc. Roy. Soc., London* 79:517, 1907; The Pressure of Pancreatic Secretion, and the Mode of Absorption of Pancreatic Juice After Obstruction of the Main Ducts of the Pancreas, *Quart. J. Exper. Physiol.* 2:99, 1909. Mann, F. C., and Foster, J. P.: The Secretory Pressure of the Liver, with Special Reference to the Presence or Absence of a Gallbladder, *Am. J. Physiol.* 47:278, 1918. Mitchell, W. T., Jr., and Stifel, R. E.: The Pressure of Bile Secretion During Chronic Obstruction of the Common Duct, *Bull. Johns Hopkins Hosp.* 27:78, 1916.

76. Harms, E.: Ueber Druckmessungen im Gallen- und Pankreasgangsystem, *Arch. f. klin. Chir.* 147:637, 1927.

ne hemorrhage is the result of a vasomotor flux; others believe that it results from venous thrombosis, and still others believe that it results from the erosion of the blood vessels by the pancreatic trypsin. Rich and Duff<sup>2</sup> found that the specific vascular lesion causing the hemorrhage was located especially in the media of the vessel, where the muscle fibers are swollen, their nuclei pyknotic and often separated by fluid spaces. The adventitia may appear condensed and pink staining and contain polymorphonuclear leukocytes. The internal elastic membrane becomes frayed, loses its undulations and takes on a swollen appearance. The first alterations of the media are found in its outer layers, the muscle fibers of which become necrotic while those near the intima remain intact. But the process is apparently a rapid one and proceeds rapidly to involve the entire thickness of the vessel wall, with final destruction of the intima. Destruction of a segment of the vessel wall was found most frequently in the larger arteries, while destruction of the whole circumference was the rule in the smaller vessels. The lesion is quite indistinguishable from that characteristic of the familiar arteriolonecrosis and hyaline arteriolosclerosis occurring in man in association with hypertension and in arteriolosclerotic nephritis.

#### SUMMARY

The historical aspects concerning the anatomy of the pancreas have been reiterated. The embryology of the pancreatic systems has been reviewed. The etiologic factors of pancreatitis have been discussed.

The anomalies and their results encountered in 250 dissections of the pancreatic systems are tabulated and discussed with their clinical significance. In 73 instances, about 24 per cent, there could be found no junction of the pancreatic and bile ducts, each entering the duodenum with

separate orifices. In 92 instances, 37 per cent, the ducts were contiguous, the dividing septum terminating 1 to 2 mm. from the apex of their common orifice. In this group, however, a true ampulla was not considered present. In 81 instances, 32 per cent, a true ampulla was present, varying in length from 3 to 14 mm., while in 4 instances, 2 per cent, the main pancreatic duct was reduced to a fibrous cord.

In 47 instances, 18 per cent, the length of the ampulla exceeded the average diameter of the duodenal orifice, and a complete block at the papilla would convert the two ducts into a communicating system.

The average diameter of the duodenal papilla was 3 mm., with limits of 1.5 and 4.5 mm.

Concerning the accessory pancreatic duct, in only 89 of 100 specimens studied for this purpose could any intraglandular communication between the ducts be demonstrated. In 4 instances, the embryonic duct system was present—i. e., the accessory duct carried the greater part of the secretion—while the main duct was reduced to a fibrous cord, leaving 85 specimens with a normal duct arrangement. In only 62 of these, 73 per cent, was the duct found to be patent, or there were 23 instances in which the accessory duct did not communicate with the duodenum, regardless of the duct arrangement, making a total of 34 per cent in which fluid could not pass from the main pancreatic duct to the duodenum by way of the accessory duct. The average diameter of the undistended duct at its point of perforation of the duodenum was 1.6 mm.

The anatomic position and arrangement of the sphincter of Oddi and the conditions modifying its resistance are discussed, and the current theories postulated regarding the necrosis and hemorrhage which occur are briefly discussed.

## SLUGGED BLOOD IN TRAUMATIC SHOCK

### I. MICROSCOPIC OBSERVATIONS OF THE PRECIPITATION AND AGGLUTINATION OF BLOOD FLOWING THROUGH VESSELS IN CRUSHED TISSUES

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This paper is the first of a series describing some studies of the pathologic circulatory physiology of animals and men preceding and during traumatic shock. The paper has two purposes: (1) to introduce this series of studies on traumatic shock and relate them to other work from our laboratories and (2) to describe the initiation of some microscopically visible changes in the physical consistency of the circulating blood which are caused by mechanical injuries to tissues (cutting or crushing injuries) but which we have not yet found caused by hemorrhage alone.

The studies of the changes in the blood, vessel walls and circulation preceding and during traumatic shock which this paper introduces are a part of a larger series of studies of normal and pathologic circulatory physiology. Our colleagues and we have been carrying out microscopic studies of:

1. The circulation in a number of tissues and organs of laboratory animals under the most nearly normal conditions which we have thus far been able to attain experimentally. (Knisely,<sup>1</sup> Bloch<sup>2</sup> and Knisely, Bloch and Warner.<sup>3</sup>)

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1. Knisely, M. H.: Apparatus for Illuminating Living Tissues and Measuring Rate and Volume of Blood Flow, *Anat. Rec. (supp.)* **58**:73 (March) 1934; (b) Mi-

2. The mechanical consistency of the circulating blood, the vasomotor behavior and the pathologic reactions of the vessel walls of the bulbar conjunctiva of (a) unanesthetized normal human beings and (b) persons with diagnoses of a wide variety of pathologic conditions and diseases (Knisely and Bloch.<sup>4</sup>).

3. The circulatory physiology of normal *Macacus rhesus* monkeys and of monkeys infected with *Plasmodium knowlesi* malaria (Kni-

croscopic Observations on Circulatory Systems of Living Transilluminated Mammalian Spleens and Parturient Uteri, *Proc. Soc. Exper. Biol. & Med.* **32**: 212 (Oct.) 1934; (c) A Method of Illuminating Living Structures for Microscopic Study, *Anat. Rec.* **64**: 499 (March) 1936; (d) Spleen Studies: I. Microscopic Observations of the Circulatory System of Living Unstimulated Mammalian Spleens, *ibid.* **65**: 25 (April) 1936; (e) Spleen Studies: II. Microscopic Observations of the Circulatory Systems of Living Traumatized Spleens, and of Dyine Spleens, *ibid.* **65**: 131 (May) 1936; (f) Microscopic Observations of the Circulatory Conditions in Living Frog Liver Lobules, *ibid. (supp.)* **73**:69 (March) 1939; (g) The Histophysiology of Peripheral Vascular Beds, in *Blood, Heart and Circulation*, American Association for the Advancement of Science, Washington, D. C. 1940.

2. Bloch, E. H.: Some Actions of Adrenalin Chloride and Acetyl-Beta-Methyl-Choline Chloride on Finer Vessels of Living Frog Liver Lobules, *Anat. Rec. (supp.)* **76**:7 (Feb.) 1940.

3. Knisely, M. H.; Bloch, E. H., and Warner, L.: Microscopic Observations of Normal Blood, Vessel Walls, and Vascular Reactions, the Testing of Methods, and the Current Development of Operative Techniques, to be published.

4. (a) Knisely, M. H., and Bloch, E. H.: Microscopic Observations of Intravascular Agglutination of Red Cells and Consequent Sludging of the Blood in Human Diseases, *Anat. Rec. (supp.)* **62**:426 (March) 1942; (b) Intravascular Agglutination of Erythrocytes in Disease, with Cinema Demonstration, *Proc. Inst. Med. Chicago* **15**:281 (March 15) 1945.

ely, Stratman-Thomas and Eliot<sup>5</sup> and Knisely, Stratman-Thomas, Eliot and Bloch.<sup>6</sup>

4. The reactions of various parts of the vascular system during and following hemorrhage initiated with a minimum amount of mechanical trauma to animals (unpublished).

5. The reactions of the blood and vascular system and the changes in the circulation following mechanical trauma made with a minimum amount of hemorrhage from animals.

Thus, we have been studying normal blood and vessel walls, surveying the condition of these in a number of diseases and trying to study the sequence of circulatory phenomena seen in hemorrhagic shock uncomplicated by trauma, the sequence in traumatic shock uncomplicated by hemorrhage, and the pathologic circulatory phenomena in *P. knowlesi* malaria uncomplicated by either trauma or hemorrhage. The over-all purposes are, of course, to recognize as many factors as possible of normal and of pathologic circulatory physiology and to determine the kinds, magnitudes and sequences of pathologic factors present in each pathologic complex.

Our studies of the changes in blood and vessel walls preceding and during traumatic shock are a direct outgrowth of the microscopic studies of the pathologic circulatory physiology of rhesus monkeys during acute *P. knowlesi* malaria (see Knisely, Stratman-Thomas, Eliot and Bloch<sup>6</sup> and the motion picture "Knowlesi Malaria in Monkeys"). As outlined in the following paragraphs, the studies on malaria provided back-

ground for and clues to follow in this series of studies on traumatic shock.

#### METHODS

Two methods are being used for studying the blood and small vessels with microscopes. One is the fused quartz rod method of illuminating living tissues for microscopic study (Knisely<sup>8</sup> and Hoerr<sup>9</sup>), which permits routine study in many internal organs of experimental animals at 32, 48, 96, 240 and 400 and less frequently at 600 diameters' magnification. The other consists in focusing stereoscopic dissection microscopes (32, 48 and 96 diameters) on the obliquely illuminated nictitating membrane and/or bulbar conjunctiva of anesthetized animals or unanesthetized human beings. A Zeiss scale in one ocular permits rapid or continuous close estimates of the dimensions of structures observed.

At all times the blood coming down the arterioles of uninjured bulbar conjunctiva is a statistically valid sample of all the flowing arterial blood in the body. This was determined by opening an animal and studying the blood passing through many different organs. In frogs, observations under various approximately physiologic and known experimentally produced pathologic conditions have been made of the vessels and blood in skin, brain, peripheral nerves, smooth muscle of the gastrointestinal tract, gastric mucosa, mesenteries, striated muscles, lung, adrenal gland tissue, kidney and liver (for operative technics see Knisely, Bloch and Warner<sup>3</sup>). In mammals, observations have been carried out in the surface of brain, omentum, mesenteries, striated muscles, smooth muscles of the gastrointestinal tract, intestinal mucosa, uterus, ovary, spleen and liver. These studies have been carried out over a fourteen year period. At any one time, the blood coming down the arterioles of all organs of an animal has the same mechanical consistency. In about 3,500 frogs, in 1,100 salamanders (*Amblystoma*), in 500 small laboratory mammals—mice, rats, guinea pigs and cats (Knisely<sup>15</sup>)—and in 50 rhesus monkeys (Knisely, Stratman-Thomas, Eliot and Bloch<sup>6</sup>), this has always been true. Hence, the blood coming

5. Knisely, M. H.; Stratman-Thomas, W. K., and Eliot, T. S.: Observations on Circulating Blood in the Small Vessels of Internal Organs in Living *Macacus Rhesus* Infected with Malarial Parasites, *Anat. Rec. (supp.)* 79:90 (March) 1941.

6. Knisely, M. H.; Stratman-Thomas, W. K.; Eliot, T. S., and Bloch, E. H.: Knowlesi Malaria in Monkeys: I. Microscopic Pathological Circulatory Physiology of Rhesus Monkeys During Acute Plasmodium Knowlesi Malaria. *J. Nat. Malaria Soc.* 4: (Dec.) 1945.

7. At several points in this paper there are references to scenes in the motion picture "Knowlesi Malaria in Monkeys." This 16 mm. Kodachrome motion picture, taken through the microscope, records several scenes of normal unagglutinated blood and normal vessel walls and then traces one set of factors of pathologic circulatory physiology through lethal stages. The picture was made to make it possible to demonstrate some of our findings to physicians and medical scientists. It usually takes about sixty minutes to project the film. Copies of this film will be loaned free, except for transportation charges, to medical schools, medical societies, medical officers of the military services and research groups. Requests should be sent either to Dr. M. H. Knisely, Department of Anatomy, University of Chicago, or to Dr. T. S. Eliot, Department of Anatomy, University of Tennessee, Memphis, Tenn.

8. (a) Knisely;<sup>10</sup> (b) The Fused Quartz Rod Method of Illuminating Living Structures for Microscopic Study, in McClung, C. E.: *Handbook of Microscopical Techniques for Workers in Animal and Plant Tissues*, ed. 2, New York, Paul B. Hoeber, Inc., 1937, pp. 632-642; (c) An Improved Fused Quartz Rod Living Tissue Illuminator, *Anat. Rec.* 71:503 (Aug.) 1938.

9. Hoerr, N. L.: Illumination of Living Organs for Microscopic Study, in Glasser, O.: *Medical Physics*, Chicago, The Year Book Publishers, Inc., 1944, p. 625.

down the arterioles of any organ, such as the uninjured bulbar conjunctiva of human beings, may be studied as a valid sample of all the flowing arterial blood in the body. This is a key fact, for it permits rather close integration of some phases of laboratory and clinical studies of normal and pathologic circulatory physiology.

By the coordinated use of these two methods, changes in the mechanical consistency of the circulating blood and the reactions of the walls of small vessels can be traced (E. R. and E. L. Clark<sup>10</sup>) with anesthetics and operations in animals and with or without anesthetics or operations in men, during phases of normal physiologic processes, during untreated pathologic processes and diseases, and during and following the administration of standard or of experimental therapeutic agents and/or procedures.

#### CONTROLS AND BACKGROUND

For a brief but clear introduction to the changes in the blood and vessel walls following mechanical trauma, which if sufficiently severe, progressive, prolonged and untreated leads to "traumatic shock," three sets of concepts are necessary: (a) concepts of normal blood and vessel walls, because clearcut concepts of the normal are necessary as a foundation for recognizing transitions into the pathologic; (b) concepts of the normal ranges of the diameters of terminal arterioles, capillaries and arteriovenous anastomoses, and (c) concepts of the changes in the blood and the vessel walls of rhesus monkeys during stage III of acute P. knowlesi malaria. Some features of the pathologic processes of traumatic shock closely parallel certain features of stage III of this malaria.

*A. Concepts of Normal Blood and Vessel Walls.*—In the internal organs of about 3,500 frogs, 1,100 salamanders (*Amblystoma*), 500 normal small laboratory mammals anesthetized with sodium amytal (Knisely<sup>18</sup>) and several normal rhesus monkeys anesthetized with pentobarbital sodium (Knisely, Stratman-Thomas, Eliot and Bloch<sup>9</sup>) and in the bulbar conjunctiva of 50 normal unanesthetized medical students and student nurses (Knisely and Bloch<sup>4b</sup>):

1. The circulating red cells were not agglutinated. Each was free from the others. They tended to repel each other slightly (Arey<sup>11</sup> and Abramson, Moyer and Gorin,<sup>12</sup> pp. 307-319).

10. Clark, E. R., and Clark, E. L.: Observations on Changes in Blood Vascular Endothelium in the Living Animal, *Am. J. Anat.* 57: 385 (Nov.) 1935.

11. Arey, L. B.: Observations on the Shape of the Erythroplasts in the Wing of the Bat, *Anat. Rec.* 14: 135 (Jan.) 1918.

2. No white cells stuck to the inner surfaces of the walls of small vessels. The inner surfaces of the linings of normal small vessels were smooth and clean. This agrees with and extends to other organs and species in the observations of E. R. and E. L. Clark.<sup>10</sup>

3. The flow of the unagglutinated blood was laminar, or "streamlined" (see Poiseuille,<sup>13</sup> figure 6, and Knisely, Bloch and Warner<sup>3</sup>).

4. The small normal vessels did not leak appreciable amounts of fluid for (a) there was no visible hemoconcentration occurring (see Krogh,<sup>14</sup> p. 14); (b) in the mesenteries and omentum of animals, the fat cells outside vessels were tight together; they were not being pushed and held apart by escaping fluid, and (c) in human beings the bulbar conjunctiva was not forced up and held away from the sclera, whereas this does occur and can easily be seen with stereoscopic microscopes in human beings at times when the bulbar conjunctival vessels are seen to be leaking rapidly.

5. The blood flowed so rapidly in most arterioles and venules which were from 60 to 120 microns in diameter that individual red cells could not be seen.

The observations of unagglutinated blood in normal human beings are particularly valuable as strict controls for animal experiments because the normal human beings had not been subjected to fright or to anesthetics or operations.

With routine care, it is possible with the fused quartz rod method to keep the exposed tissues and organs of normal rhesus monkeys anesthetized with pentobarbital sodium under continuous observation for fourteen to eighteen hours without causing any of the microscopically visible evidences of injury to the blood (see the following sections) or vessel walls (E. R. and E. L. Clark<sup>10</sup>). Normal unagglutinated circulating blood and normal vessel walls of monkeys have been recorded in motion pictures (see reel 1 of the Knowlesi Malaria film<sup>7</sup>).

*B. The Diameters of the Smallest Vessels.*—In most organs of a number of mammalian species, those capillaries through which blood is flowing normally vary from a little more than

12. Abramson, H. A.; Moyer, L. S., and Gorin, M. H.: *Electrophoresis of Proteins and Chemistry of Cell Surfaces*, New York, Reinhold Publishing Corporation, 1942.

13. Poiseuille, J. L. M.: *Recherches sur les causes du mouvement du sang dans les vaisseaux capillaires*, Mém. Acad. d. sc., Paris 7:105, 1841.

14. Krogh, A.: *The Anatomy and Physiology of Capillaries*, ed. 2, New Haven, Conn., Yale University Press, 1929.

once to a little more than twice or even two and a half times the diameter of the red cells which pass through them. The red cells usually pass in single file or, at most, a double row. When a capillary contracts or is compressed to just a little less than the diameter of the contained red cells, the red cells rub on the inner surface of the endothelium and thus resist passage, and the flow through that vessel soon stops (see Krogh,<sup>14</sup> page 11, and Knisely<sup>15</sup>). Most true capillaries can dilate without losing tonus, weakening and sacculating to a little more, but usually not much more, than two or two and a half times the diameter of the contained red cells (Krogh,<sup>14</sup> p. 335, and Knisely, Stratman-Thomas, Eliot and Bloch<sup>6</sup>). The arterioles of most of the organs in frogs and mammals which we have studied are long, narrow, tapering cones. During the flow of blood through them, their outlet tips vary either anatomically or functionally from a little wider to a little narrower than the capillaries or sinusoids they join and supply. These statements are true of the arterioles and capillaries of the bulbar conjunctiva of human beings and almost certainly true of the arterioles and capillaries of many other human organs during life. Arteriovenous anastomoses have thus far been found in but a few organs of any one species. The arteriovenous anastomoses which have been found are often closed and when open are frequently but two or three times the diameter of the red cells passing through them (see the reviews by E. R. Clark<sup>15</sup> and Boyd<sup>16</sup>). These are key points for understanding some of the pathologic processes initiated by intravascular agglutination of the blood, for they show that most of the time, under most conditions, nearly all the circulating blood must pass through vessels having an internal diameter from about once to twice or at most three times that of the red cells on every trip from the left side of the heart through the circulatory system and return. Thus, as is well known but not always remembered, the arterioles and capillaries are a perpetual "bottleneck" in the vascular system.

*C. Some Changes in the Blood and Vessel Walls During Stage III of P. knowlesi Malaria.*—At the beginning of stage III of the pathologic circulatory physiology of rhesus monkeys with *P. knowlesi* malaria, a thick, glassy precipitate forms between and around all the blood cells of the animal. In this malaria, this

precipitate forms throughout all of the animal's circulatory system at one time. The process acts as though it were autocatalytic; once it starts, it usually goes on to completion in from ten to about twenty minutes. This precipitate binds the animal's red cells together in wads and masses (*not rouleaux*), which by microscopic standards are large, semirigid and tough, and thereby rapidly changes all the animal's circulating blood into a thick, mucklike sludge.

As soon as the blood has changed to this thick, pasty sludge, a definite sequence of events takes place. Three major steps are as follows:

1. This sludge resists its own passage through small vessels much more than does normally fluid blood; consequently, the rate of flow through small vessels all over the body becomes progressively slower than the normal rates for each degree of dilatation of each vessel. This increased resistance to flow and consequent reduced rates of flow through the capillary beds slowly, progressively and inescapably leads to various degrees of stagnant anoxia all over the body.

2. There is a time interval of variable length during which (a) the reduced rates of flow are unmistakable and (b) there is still no visible hemoconcentration of the sludge passing through peripheral vascular beds. During this period, the flow through each small vessel is slower than the normal rate for whatever degree it is dilated but the vessels have not yet begun to leak perceptibly (see the scenes following titles 29, 30 and 31 in the Knowlesi Malaria film<sup>7</sup>). After the sludged blood has been flowing too slowly for a time, the walls of postcapillary venules and small venules lose their ability to retain blood colloids. Anoxia of the endothelium is alone sufficient to cause this (see Starr<sup>17</sup>; Starling<sup>18</sup>; Landis<sup>19</sup>; Krogh,<sup>14</sup> pp. 321, 326 and 335; Maurer<sup>20</sup>; Warren and Drinker<sup>21</sup>; Drinker,<sup>22</sup>

17. Starr, I., Jr.: Production of Albuminuria by Renal Vasoconstriction in Animals and Man. *J. Exper. Med.* **43**: 31 (Jan.) 1926.

18. Starling, E. H.: *Principles of Human Physiology*, ed. 4, Philadelphia, Lea & Febiger, 1926, p. 854.

19. Landis, E. M.: Micro-Injection Studies of Capillary Permeability: III. The Effect of Lack of Oxygen on the Permeability of the Capillary Wall to Fluid and to the Plasma Proteins, *Am. J. Physiol.* **83**: 528 (Jan.) 1928.

20. Maurer, F. W.: The Effects of Decreased Blood Oxygen and Increased Blood Carbon Dioxide on the Flow and Composition of Cervical and Cardiac Lymph. *Am. J. Physiol.* **131**: 331 (Dec.) 1940; The Effects of Carbon Monoxide Anoxemia on the Flow and Composition of Cervical Lymph, *ibid.* **133**: 170 (May) 1941; The Effects of Anoxemia Due to Carbon Monoxide

15. Clark, E. R.: Arterio-Venous Anastomoses, *Physiol. Rev.* **18**: 229 (April) 1938.

16. Boyd, J. D.: Arterio-Venous Anastomoses, *London Hosp. Gaz. (Clin. Supp.)* **42**: i (July) 1939.

and I. Bloch,<sup>23</sup> and in a variety of unpublished experiments of ours sufficiently severe anoxia always caused endothelium to leak fluids rapidly. The larger and more rigid the masses of precipitate-coated agglutinated blood cells, the more they resist passage through the long, cone-shaped arterioles and the capillaries, the slower the flow through the peripheral vascular beds and the shorter the period before the vessel walls begin to leak perceptibly.

3. Postcapillary venules and small venules begin to leak fluid, at first slowly and later more rapidly. The vessels of some tissues and organs begin to leak before those of others. Hence, local areas begin to lose fluid, and in these local areas continuous microscopically visible hemoconcentration begins (see Krogh,<sup>14</sup> p. 14, and the scene following title 35 in the Knowlesi Malaria film<sup>7</sup>). At first the fluid being lost through the walls of postcapillary venules and small venules can be returned to the blood vascular system by way of lymphatics as fast as it is lost. Later, rapid local fluid losses and local hemoconcentrations occur all over the body, and, finally, as a result of rapid local fluid losses, enormous numbers of small vessels are left plugged with stranded masses of precipitate-coated, tightly agglutinated blood cells.

As a result of these processes, the sum of the rates of local fluid losses becomes greater than the sum of the rates of return of fluids to the blood by lymphatics. Hence, at the same time that enormous numbers of small vessels are being plugged with stranded masses of coated, agglutinated red cells, there is a progressively decreasing intravascular plasma volume. The stranding of precipitate-coated masses of red cells in small vessels and fluid loss from small vessels are major factors causing a progressively decreasing circulating blood volume and venous return (see Knisely, Stratman-Thomas, Eliot and Bloch<sup>6</sup> and reel III of the Knowlesi Malaria film).

When fine droplets of india ink are injected into the blood stream of frogs, each small droplet

and Low Oxygen on Cerebrospinal Fluid Pressure, *ibid.* 133:180 (May) 1941.

21. Warren, M. F., and Drinker, C. K.: The Flow of Lymph from the Lungs of the Dog, *Am. J. Physiol.* 136:207 (March) 1942.

22. Drinker, C. K.: The Lymphatic System, Stanford University, Calif., Stanford University Press, 1942, pp. 78-84.

23. Bloch, I.: Some Preliminary Considerations Concerning Concentration of Oxygen in Tissue, *Bull. Mathemat. Biophysics* 3:121 (Dec.) 1941; Some Theoretical Considerations Concerning the Interchange of Metabolites Between Capillaries and Tissue, *ibid.* 5:1 (March) 1943.

immediately receives a complete coating of a clear, glassy precipitate formed from the frog's plasma. This coating is not sticky to the red cells it bumps or to ordinary undamaged vascular endothelium, but it is extremely sticky to the inner surface of the sinusoid-lining Kupfer cells of living frog liver. When and wherever this coating material touches the inner surface of the hepatic sinusoid lining, it sinks with its contained ink into the cytoplasm of the lining. The ingestion of a bit of this coating appears to be as fast as that when a small sphere of mercury touches and merges with and into a larger one (see Knisely, Bloch and Warner<sup>24</sup> for more details). During stage III of *P. knowlesi* malaria in monkeys, coatings are precipitated around normal circulating red cells, and these coatings are ingested with the contained erythrocytes by the phagocytes of the liver, bone marrow and spleen. In monkeys, the rapid ingestion of coated erythrocytes (a) contributes to decreased red cell counts (anemia) and (b) assists in progressively decreasing the circulating blood volume.

In summation, the controls and background for the subsequent observations of the effects of mechanical trauma are:

1. In normal animals and men, the blood cells are not agglutinated, the red cells repel each other slightly and the white cells do not stick to vessel walls. The walls of capillaries, postcapillary venules and venules do not leak rapidly enough to be detected by microscopic observation.

2. Most of the time, under most conditions, nearly all the circulating blood must, because of the anatomy and dimensions of the peripheral parts of the living vascular system, pass through vessels having an internal diameter from about once to twice or at most three times that of the red cells on every trip around the circulatory system.

3. In monkeys with *P. knowlesi* malaria, at the beginning of stage III, (1) a precipitate is formed between and around all the blood cells, coats them and binds them together in great semirigid wads and thereby changes all the circulating blood to a thick, mucklike sludge. The formation of this particular malaria sludge usually takes but ten to twenty minutes. (2) The heavily sludged blood flows more and more

24. Knisely, M. H.; Bloch, E. H., and Warner, L.: Selective Phagocytosis: I. Microscopic Observations of the Selective Phagocytic Removal of Coated Particles from Flowing Blood by the Sinusoid Lining Cells of Living Frog Liver, to be published.

slowly, but for a time the walls of vessels do not leak perceptibly. (3) When the flow has been slow enough for a long enough time, post-capillary venules begin to leak, at first slowly and then more rapidly. (4) Venule walls leak so rapidly that masses of coated cells are left stranded in the vessels. (5) The stranding of coated masses in vessels and loss of fluid from vessels causes a progressively decreasing circulating blood volume and venous return. (6) The rapid ingestion of coatings containing erythrocytes by the phagocytes of liver, bone marrow and spleen acts toward causing and maintaining (a) low red cell counts (anemia) and (b) progressively decreasing circulating blood volume.

*How Studies of Malaria Led to Studies of Traumatic Shock.*—When the formation of the stage III precipitate was seen with the microscope in a living monkey infected with *P. knowlesi*, the chemical and immunologic natures of the precipitate immediately became important problems. Consequently, samples of this heavily sludged stage III blood were drawn into oiled and heparinized or oiled and citrated syringes, injected into little petrolatum-ringed pools of citrated mammalian Ringer solution on microscope slides and examined by direct light and by dark field illumination.

In the living animal, all the red cells were held together in wads and masses. On the slide, not more than two minutes afterward, some clumps had separated; the rapid, forcible swirling of the blood as it passed into and out of the syringes and/or the solutions used caused many clumps to disintegrate into individual red cells. However, many masses of clumped red cells remained. By transillumination in vitro, the material which held these clumps together was not visible. By dark field illumination, it was obvious that a thick, glassy, cottony precipitate was present between and around all the red cells of each clump. (This is shown in the Knowlesi Malaria film following title 48 a).

Bloch pulled some of these clumps apart with a Chambers microdissector (see Chambers and Kopac,<sup>25</sup> pp. 62-109). The precipitate which held the erythrocytes together was fairly abundant and had a stringy or gluey or tarry consistency. By microscopic standards, it was rather tough. The appearance and consistency of the precipitate suggested that it might be largely

fibrin or some fibrin-like material. Consequently, we decided to try to form some fibrin within the vascular system of a normal monkey to see what freshly formed, intravascular fibrin would look like in the living animal.

#### MICROSCOPIC EXPERIMENTS WITH MECHANICAL TRAUMA

*I. Experimental Crushing of Monkey Omentum.*—A young, vigorous male monkey was selected and anesthetized with pentobarbital sodium given intrapleurally.<sup>26</sup>

When the animal was asleep, an eyelid was reflected (its tarsal plate keeps it flat) and the reflected portion transilluminated with a fused quartz rod to permit microscopic study of the circulating blood and the vessel walls of the inner surface of the eyelid. This area was than studied at 32, 48 and 96 diameters to see whether the blood and the vessel walls were normal. During these observations, made to help select a normal experimental animal and as controls for possible effects of the laparotomy which followed, the vessel walls and the blood flowing in them looked perfectly normal, for (a) the circulating red blood cells were not agglutinated, (b) each red cell which bumped a vessel bifurcation turned over easily, demonstrating that the plasma viscosity was within the normal range, (c) no white cells were sticking to the walls of small vessels, (d) no visible hemoconcentration was occurring in any small vessel, (e) there were no emboli in this area and no minute thromboses and (f) the flow of the normal unagglutinated blood in small venules was laminar, or "stream-

26. We did not want an anesthetic solution in high concentration on omental tissues which were to be observed with microscopes, and the rates of absorption from subcutaneous fascias are irregular and unpredictable. Solutions of crystalloids are absorbed rapidly from the pleural space, probably because (a) the outer surface of the lung has great numbers of capillaries, (b) the lateral pressure within lung capillaries is much less than that of the inwardly directed oncotic "attraction" force of the dissolved blood proteins, (c) the flow through these vessels is rapid and (d) there is a continuous mixing and spreading of films of fluid in the pleural space due to the respiratory excursions of the lung. Hence, the pentobarbital sodium was given intrapleurally.

The calculated dose of pentobarbital sodium is divided into fourths. At first, two quarter-doses are given; after fifteen minutes, the third quarter, and after fifteen minutes more, the fourth quarter-dose. A fifth quarter-dose is given later if necessary and an additional quarter-dose or eighth-dose given whenever necessary. This maintains a controlled, nearly even anesthesia. Care must be taken (a) to avoid the intercostal arteries and veins to prevent hemorrhage (a small needle [no. 27] is less apt to injure an artery than a large one), (b) to be sure to go all the way through the intercostal muscles and reach the intrapleural space and (c) to be sure not to injure the lung. As the lung has a wide respiratory excursion, it can be snagged on an inwardly projecting needle; the needle should not be pushed in any farther than necessary. We ground needle tips off a little to a smooth, rounded point, which can be pushed through the skin and muscle but is more apt to indent than to cut the resilient lung tissue.

25. Chambers, R., and Kopac, M. J.: *Micrurgical Technique for Study of Cellular Phenomena*, in McClung, C. E.: *Handbook of Microscopical Techniques for Workers in Animal and Plant Tissues*, ed. 2, New York, Paul B. Hoeber, Inc., 1937, pp. 62-109.



lined." Thus, these observations did not detect any abnormality of the circulating blood or vessel walls.<sup>27</sup>

The monkey was then opened, with minimal blood loss, by a median abdominal incision, and a fold of omentum was gently drawn out and a portion spread over a horizontal loop of stiff, paraffin-coated copper wire. The loop supported an area of omentum  $1\frac{1}{2}$  inches (3.8 cm.) in diameter and held this area a short distance from the abdomen. The intervening omentum was left slack so that the animal's respiratory movements were not transmitted to the supported omentum.

The exposed omentum was protected with flowing (Knisely<sup>28</sup>) mammalian Ringer solution at body temperature and the tip of a quartz rod illuminator brought up under the supported area so that portions of it could be studied with microscopes. The whole supported area was then studied microscope field by microscope field at 32, 48 and 96 diameters. During these control observations, the blood and vessel walls were normal, according to each of the criteria previously listed. Thus, no single factor or combination of factors of the anesthetic, the laparotomy, the withdrawing of the omentum and the transillumination of the area were sufficiently injurious to cause any of the known microscopically visible reactions of blood or vessels to injury (E. R. and E. L. Clark<sup>10</sup> and Knisely, Bloch and Warner<sup>2</sup>).

There were a few small injured vessels at the periphery of the supported area where the omentum had been bumped against the paraffined wire. These showed the pathologic stasis described by Florey<sup>28</sup> and Krogh,<sup>14</sup> p. 14.

In the omentum of *Macacus rhesus* monkeys, each small artery is accompanied by its own small vein. Pairs of these run close together for long distances. Large, powerful arteriovenous anastomoses interconnect the members of these pairs. There are so many of these arteriovenous anastomoses that, except for the capillary beds of small lymph nodes, each of which has its own blood supply, all the capillary networks of the omental tissue can be short-circuited at once. Sometimes all the arteriovenous anastomoses open and the capillaries constrict tightly shut throughout their lengths, ejecting their contents, and then contain no blood (see Krogh,<sup>14</sup> pages 47 to 69) and there is a rapid flow through the dilated arterioles, arteriovenous anastomoses and venules of the whole omentum. The omental vessels of this animal went into this reaction and maintained it for the rest of the period of this experiment.

An area about 3 mm. in diameter was selected at a point where an arteriovenous anastomosis joined the side of a small vein (see the figure). The tip of the quartz rod, which was about 2.5 mm. in diameter, was brought from beneath up into contact with this area, the dis-

section microscope was focused on the tissue and the area was then crushed by pushing and rubbing it gently against the end of the rod with the tip of a forefinger. The quartz rod is supported on springs (see Hoerr<sup>9</sup> for diagram); hence, it is not possible to exert much force on the tissue by pushing the omentum against the rod. The tissue was pushed against it gently and rubbed back and forth a millimeter or two, two or three times.

There were ten significant results, as follows:

1. As the finger was removed, it was found that the blood flowing through the dilated arteriovenous anastomosis (see fig.) was changing from its normally fluid state to a rather stiff sludge. Fluid blood continually came in the arterial end of the vessel, and as it passed along a somewhat viscid glassy precipitate formed between and around the red cells of the moving column. This precipitate filled the space between the red cells and, like the mortar between bricks, simultaneously held them apart and held them tightly together. Thus, the fluid blood was continually precipitated into masses of pasty sludge as it passed through this vessel of the gently crushed omental tissue. These masses were not rouleaux, although short rouleaux were often contained in them. The masses were groups of red cells bound together at all angles to each other by a nearly transparent, faintly straw-colored material. By microscopic standards, this material was very viscid and coherent. For at least an hour, all the blood passing through this vessel changed to a sludge as thick as freshly formed stage III *P. knowlesi* malaria sludge. The arteriovenous anastomosis was dilated to a little less than twice the diameter of the monkey's red cells; the pressure in it was high and the flow through it very rapid. Thus, for at least an hour one small vessel of the injured area was pouring a continuous rapid small stream of thickly sludged blood into the general circulation.

2. One small venule (*Th* in the figure) was thrombosed. It was solidly plugged with a mass of precipitate and red cells formed while the area was being crushed. This vessel had no flow through it; consequently it was not pouring sludge into the vascular system.

3. Other small vessels but a few tenths of a millimeter from the crushed area contained normal blood flowing normally.

4. No vessel wall ruptured; there was no diapedesis of red cells or hemorrhage into this particular injured area.

5. There was no visible hemoconcentration of the red cells passing along any of the vessels of this area; these local vessels were not leaking

27. This method of preselecting normal animals by microscopic observations before beginning experiments was instituted because we had found precipitated-agglutinated, circulating red and white blood cells in a supposedly normal monkey. At autopsy that animal was found to have pulmonary tuberculosis. Human beings with pulmonary tuberculosis have one form of sludged blood. An animal with microscopically visible pathologic conditions of its vessel walls or precipitated-agglutinated circulating blood cannot be considered a normal experimental animal (Clark and Clark,<sup>10</sup> Knisely and Bloch,<sup>4</sup> Knisely, Bloch and Warner<sup>2</sup>).

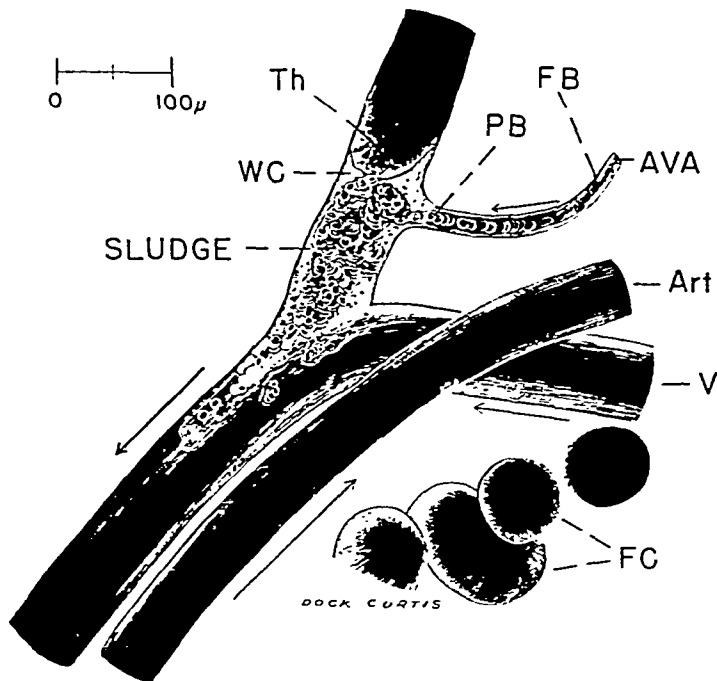
28. Florey, H.: Observations on the Resolution of Stasis in the Finer Blood Vessels, *Proc. Roy. Soc., London*, s.B 100:269 (Sept.) 1926.

significantly, probably because all the vessels of the area were by microscopic standards fairly large; arterioles, arteriovenous anastomoses and venules of this size have substantial smooth muscle coats.

6. At the moment the finger was removed from the tissue, few if any white cells were sticking to the walls of injured vessels. However, many of those brought in by the flowing blood adhered to the injured walls. Hence, in a few moments white cells had accumulated one or two and even three layers deep and in irregular masses on injured endothelial surfaces (see the figure and consult E. R. and E. L. Clark<sup>10</sup>).

to determine the precipitation rate (Nygaard<sup>29</sup>), and (c) to record the scene for further study. The scene is somewhat underexposed, satisfactory for research purposes or private showing but not for general distribution.

Copies of this film were later spliced into loops for continuous projection to permit several persons to study the scene together, repeatedly, detail by detail. The outline of the figure is a ciné tracing of the scene, made by projecting the film onto a large sheet of drawing paper while an artist traced the outlines of the stationary structures (Brown and Sheard<sup>30</sup>). Thus these outlines and the scale have about the same accuracy as a good camera lucida drawing. The



Ciné-tracing of a motion picture of blood flowing through crushed monkey omentum. Art, artery; V, vein; AVA, arteriovenous anastomosis; FC, fat cells; Th, thrombosed venule; WC, masses of white cells stuck on inner surface of injured venule; FB, fluid blood; PB, precipitated blood, and SLUDGE, masses of precipitated-agglutinated blood. Note the scale in upper left. Arrows show direction of blood flow. The details of the precipitated-agglutinated blood were added by the artist while studying a looped continuous projection of the scene.

The adhering masses of white cells were continually being bumped by wads of the rapidly moving sludge; from time to time masses of these white cells were forced loose from the vessel lining and carried downstream to the general circulation.

This microscope field was then photographed on Kodachrome motion picture film at 24 frames per second and a Zeiss microscope scale photographed with the same lens combination, in order (a) to measure the dimensions of the structures present, (b) to find out how long it was taking fluid blood to change to thick pasty blood, i. e.,

following additional results were obtained from studies of the film.

7. The blood was fluid at point FB and rather solidly precipitated at PB. The precipitation end point is not exact, however, nor exactly determinable from the scene. Nor was the precipitation rate constant. Sometimes fairly solid precipitates were formed in blood which had

29. Nygaard, K. K.: Hemorrhagic Diseases—Photo-Electric Study of Blood Coagulability, St. Louis, C. V. Mosby Company, 1941.

30. Brown, G. E., and Sheard, C.: Measurements of the Skin Capillaries in Cases of Polycythemia Vera and the Role of These Capillaries in the Production of Erythrocytosis, J. Clin. Investigation 2: 423 (June) 1926.

passed but halfway from *FB* to *PB*. No blood passed *PB* in the fluid state. Thus all the blood changed from a fluid to a precipitated sludge as it moved approximately 100 to 150 microns.

8. By counting the motion picture frames during which a group of blood cells passed from *FB* half or all the way to *PB*, it was found that the precipitation occurred in from one eighth to one fourth of a second. This shows how fast such precipitates can form in a living animal (consult Nygaard<sup>29</sup>); it does not, of course, mean that all such precipitates are formed so rapidly.

9. As the precipitated masses formed, some of them rounded up between points *FB* and *PB* and forcibly bulged the arteriovenous anastomosis; this is evidence that they were rather rigid, for an arteriovenous anastomosis of this size has a fairly strong smooth muscle wall, and at this time this one was partially contracted, i. e., in a tonic, not a flaccid, state.

10. The motion picture shows clearly that as the precipitated masses passed out of the arteriovenous anastomoses they stuck together and rapidly piled up into larger cohering masses. Thus the outer surface of the freshly formed precipitate was sticky to itself. Fragments of these large masses were intermittently torn off by the flowing blood and carried away. At short intervals whole large masses passed into the efferent venule. Occasionally masses of white cells were carried away. From the outlet orifice of the arteriovenous anastomosis, the sludged blood continually spewed out, piled up, agglutinated and passed on.

*Interpretations.*—Obviously, at this point this experiment can be appraised (1) according to its original purpose as a part of the malaria studies, an attempt to see what freshly formed fibrin might look like in the circulating blood, and (2) as an introduction to studies of the reactions of blood flowing through or beside injured tissues.

Looking at this experiment as a part of the malaria studies, one can conclude that a material which could be fibrin or related to fibrin looks and behaves much like the stage III *P. knowlesi* malaria precipitate, and in consequence all malaria precipitates should be examined both chemically and immunologically (some fibrinogens exhibit group and/or species specificities [Hektoen and Welker,<sup>31</sup> Kyes and Porter<sup>32</sup> and

Kenton<sup>33</sup>]) to determine their relationships to the fibrins.

About the time these observations were made, Dr. Harrison Rigdon pointed out in a seminar on malaria that monkeys dying of *P. knowlesi* malaria sometimes presented conditions at autopsy similar to Prof. Virgil Moon's<sup>34</sup> descriptions of the observations at autopsy in cases of traumatic shock (see Moon's 1942 summary and compare the findings he presented in his chapters IX and XI). Sludged blood occurs in a variety of pathologic conditions and diseases of human beings (see Knisely and Bloch<sup>4</sup>). Whenever the blood is sludged, the decreases in the rates of flow through small vessels, caused by the resistance of the masses of the sludge to passage through the smallest vessels, are a function of the mechanical consistency of the sludge which is present. Given a normal arterial pressure, the decreased rates of capillary flow caused by sludged blood are only indirectly and in part a result of the chemical sources of the sludge; the decreased flow rates are a direct result of the mechanical consistency of the sludge which is present. Thus sludges need not have identical chemical compositions to produce similar effects on (a) circulation rates and, consequently, (b) rates of supply of oxygen to endothelium.

Hence, the concepts about mechanisms causing death in monkeys during stage III of *P. knowlesi* malaria just outlined, Moon's accounts of the observations at autopsy in cases of traumatic shock and the described observations in crushed monkey omentum suggested a working hypothesis about mechanisms which might cause death after crushing injuries.

Seen as possible initiating factors in traumatic shock, the observations made in that microscope field in monkey omentum may be summarized as follows:

In this one tissue:

1. Crushing plus flow through a vessel in the crushed area yields a stream of sludge into the general circulation.

2. Crushing plus thrombosis of a crushed vessel yields no sludge to the venous system.

3. Flow without crush yields no sludge.

Thus, after trauma, (a) local crush and (b) flow through a vessel in the crushed area are both necessary and together are sufficient to yield a flow of sludged blood into the general circulation.

33. Kenton, H. B.: Species Specificity of Fibrinogens. *J. Immunol.* 25: 461 (Dec.) 1933.

34. Moon, V. H.: Shock: Its Dynamics, Occurrence, and Management, Philadelphia, Lea & Febiger, 1942.

31. Hektoen, L., and Welker, W. H.: The Precipitin Reaction of Fibrinogen, *J. Infect. Dis.* 40: 706 (June) 1927.

32. Kyes, P., and Porter, R. T.: The Antigenic Properties of Fibrinogens, *J. Immunol.* 20:85 (Feb.) 1931.

4. For a time after the crush, the rate at which sludge is poured into the venous system can be as fast as the rate of flow through an open vessel in the crushed area.

5. This sludge can be formed in an area from which or into which there is (a) no hemorrhage and (b) but little loss of plasma through injured vessel walls.

6. When first formed, some of the masses have sufficient internal rigidity to bulge the walls of the vessel through which they are being forced; if not changed, such masses would resist passage through capillaries.

7. When first formed, the outer surfaces of the precipitated material are sticky to each other; hence, if not changed, masses coated with this material must, whenever they touch each other, tend to stick together and form larger masses.

8. The precipitated material contains erythrocytes and may be ingestible by the phagocytes of spleen, bone marrow and liver. If the material is phagocytosed, the contained erythrocytes would be removed from the circulatory system and destroyed.

*Working Hypothesis.*—Putting these bits together, one can formulate a working hypothesis about mechanisms which might cause death after crushing injuries. This hypothesis can perhaps best be stated as a set of general questions, as follows:

1. Can the crushing of tissues cause the release of substances from the crushed tissues which can cause the precipitation and agglutination of blood flowing through or beside the crushed tissues?

2. Can the crushing of gross regions of the human body or of specific tissues or organs initiate processes which can change all the circulating blood to a sludge whose masses are large enough and rigid enough to retard the flow in small vessels enough to cause them to become anoxic and leak?

3. From crushing injuries alone, can the circulating blood be changed to a sludge which resists flow through small vessels enough to cause rapid local fluid losses all over the body, plugging of vessels with agglutinated masses, decreasing circulating blood volume, failure of venous return and death?

4. Following trauma, does rapid ingestion of coatings containing red cells by the phagocytes of liver, bone marrow and spleen (a) contribute to decreasing the total numbers of circulating red cells and (b) assist in causing progressively decreasing circulating blood volume?

5. In many injuries, hemorrhage and trauma are of course both present. Can these sludge mechanisms contribute to the decreased venous return in animals and human patients who have suffered combinations of hemorrhage and trauma?

These five questions define the broad outlines of the problem. Note that the questions deal with (a) concepts of chemical reactions, (b) concepts of degree and (c) concepts of rates. The rest of this paper is an attempt to find the beginnings of the answers to the first of these questions.

#### *Reflections About the First General Question.*

—Consider the first general question in the aforementioned series. Obviously this question needs subdividing, for it contains or implies questions such as these:

Are the precipitation and agglutination of the blood flowing past the injury due to the liberation of one or more diffusible substances from injured tissues? Is the same diffusible substance released from each crushed tissue? What factors determine the rates of release of the diffusible substances? If such diffusible substances are released from injured tissues, do they always react and then become inactive at or very near the site of injury, or may they be carried in the circulating blood for a time and act later, after they have accumulated to or above some threshold concentration? That is, may some one or more of such diffusible substances act immediately and some accumulate in solution in the circulating blood for a time after an injury and later initiate changes in the mechanical consistency of the circulating blood?

These questions cannot at present be tested directly, but, as a first step in finding the answers to them, the following questions can be asked, each of which can be tested by direct methods.

(a) Which tissues or organs cause sludging of the blood after they are crushed?

(b) What are the characteristics of the sludge produced by the crushing of each tissue? Are the sludges thus produced alike or visibly different?

(c) How slight an injury causes sludging of the blood passing the injured area?

(d) What degree of severity of injury is present after tissue is crushed? What happens after each?

(e) For how long a time after a tissue is crushed does the sludging of the blood continue? What factors determine the duration of this process?

(f) What factors determine and limit the rates of production of sludge and the duration of the production of sludge after a mechanical injury?

*II. Experimental Crushing of Mouse Striated Muscle.*—The purpose of this experiment was to find the effects of slight trauma to a muscle.

An adult male mouse was anesthetized with 1.2 mg. of pentobarbital sodium in 0.4 cc. of water given subcutaneously. Its fur was then brushed lightly with a little petrolatum to (a) hold the ends of the hairs together to prevent cut hairs from being blown onto the exposed tissues and (b) to cause the animal to shed the Ringer solution escaping from illuminated areas. A cut was made with scissors through the skin transversely across the anterior abdominal wall about halfway between the xiphoid process and the symphysis pubis, and a midline incision led from this back toward the pubis. The skin retracted in all directions by its own elasticity, exposing a roughly triangular area of the lower abdominal musculature. During the cutting, the scissors were closed slowly, a procedure which crimps and thromboses small cut blood vessels, thus decreasing the number of small hemorrhages (Knisely, Bloch and Warner<sup>24</sup>). The cut edges of the skin were examined by reflected light at 32 diameters for clots and hemorrhages. One small arteriole had bled enough to yield a clot shaped like a doubly convex lens, about 2 mm. in diameter and 0.5 mm. thick; otherwise no blood was lost. The surface of the exposed abdominal musculature was then examined at 32 and 48 diameters to see whether the operation had initiated precipitation and agglutination of blood flowing through small vessels of the area. No sludge was seen, probably owing to our inexperience; many times since then we have seen sludging of the blood passing through some of the superficial vessels of such freshly exposed areas.

By cautery, a paramesial slit about 4 mm. long was made bloodlessly through one side of the exposed muscle. The quartz illuminator tip was then inserted through this slit and an area of striated muscle brightly transilluminated for microscopic study. The musculature of the lower anterior body wall was about 1 to 2 mm. thick. Thus this preparation provided several square centimeters of thin, nearly intact, living striated muscle for experiments.

The small vessels within the muscle itself, which are deeper than the superficial vessels and thus less exposed to injury during retraction of the skin, were then examined at 48 and 96 diameters for evidences of trauma; none were seen. The vessel pattern is that described in striated muscle by Spalteholz in 1888.<sup>35</sup> The blood flowing through the arterioles, capillaries and venules of the muscle was not agglutinated; the red cells were all free from each other; no white cells were sticking to vessel walls, nor did the walls exhibit any pathologic dilatations or sacculations. There was no visible hemocentration of the blood flowing through any of the vessels of this muscle, and no small hemorrhages, clots, thrombi or emboli were present in the muscle. These observations are the first controls for the following experiments.

Next, a small area of the muscle was traumatized as gently as could be done without special microdissection

equipment. To do this, the illuminator tip was raised against the inner surface of the muscle and then the muscle directly over the tip was compressed and partly crushed with one firm wiping motion of a small, smooth, round-edged forceps handle. The injured area was about 3 mm. in diameter; the muscle was about 1 mm. thick at this point.

As noted, the injury was kept as slight as possible. When the forceps handle had passed, the muscle was not left crushed out of shape, as after the removal of a hemostat. As the pressure was removed, the muscle fibers assumed their normal cylindric shapes again; they showed no visible injuries at 96 diameters' magnification. The muscle was injured at 4:30 p. m. The injured area was then observed continuously for the duration of the experiment, four hours and ten minutes.

Results: Immediately after the trauma there were three clearly recognizable zones as follows:

1. Two postcapillary venules in the center of the injured area were plugged with a precipitated-agglutinated mass formed during the injury. No blood was passing through these vessels; hence they were not pouring sludged blood into the general circulation.

2. The afferent capillary ends of all other small venules in the injured area were receiving normally fluid blood, and precipitated-agglutinated (sludged) blood was flowing from their efferent ends into the next larger venules. The red cells could easily be seen agglutinating into firm masses as they passed through the venules in the damaged area. This was a very slight injury, yet all the blood flowing through the injured area was coming out as sludged blood. The sludged blood did not seem to flow much more than one fourth as fast as did the normal blood in vessels of comparable size in adjacent uninjured areas. White cells were sticking to the walls of those venules in the damaged area through which blood was flowing. Groups of them amassed and then broke loose and were carried downstream. Irregular dilatations, bulges and sacculations developed in the walls of injured vessels, but the walls did not weaken enough to permit diapedesis of red cells or hemorrhages (E. R. and E. L. Clark<sup>20</sup>).

3. The blood flowing through the vessels of the contiguous, untraumatized muscle and through untraumatized muscle in neighboring microscopic fields was as normal as before. (This is both an observation and a control.)

The sludge being formed in the slightly injured mouse muscle did not have the same consistency as that formed in the crushed monkey omentum; the clumps or red cells were smaller, more fragile and less sticky to each other than those formed in the monkey omentum.

35. Spalteholz, W.: Die Vertheilung der Blutgefäße im Muskel, Abhandl. d. math.-phys. Cl. d. k. säch. Gesellsch. d. Wissensch. 14:507, 1887-1888.

At 6 p. m., ninety minutes later, the following observations were made: 1. The plugs were still present in the two thrombosed venules. 2. The damaged area was still pouring sludged blood into the smaller veins which drained it. A point was found where a venule which came from the damaged area joined one which came from an area of undamaged muscle. Here the experiment and the control were present in one microscope field; it was easy to compare the sludged and the normal blood. There were no free individual cells in the blood passing out of the venule draining the damaged area; all this blood was precipitated and agglutinated into a sludge. 3. No two red cells were sticking together in the blood from the uninjured area; all were free, each turned over by itself unattached to any other—that is, normal blood was flowing through normal vessels in adjacent untraumatized areas of the muscle.

At 6:15 p. m. blood passing through the injured area was still changing to a sludge. At this time, however, there began to be a change. Some of the smallest venules in the injured area had almost normal blood for a few minutes and then sludged blood again. The sludge was being formed intermittently, and the sludge being formed was softer, i. e., the clumps had a fluffy, feathery character rather than a firm, rigid texture. The area was still pouring sludge into the venous system, but there had been a definite decrease in rate of production of sludge, and that produced might better be called a "slush" than a sludge.

It seems reasonable to assume that whatever had been initiating the production of sludge was not reaching or acting in the blood flowing through the injured area as rapidly as during the first ninety minutes after injury.

At 6:30 p. m. the following observations were made. 1. The plugs were still present in the two thrombosed venules. 2. The blood flowing through the injured area was still changing consistency. The sludge formed was less pasty than that formed at first. It was softer, the clumps were more plastic and the rates of flow through these vessels were increasing, approaching the rates through vessels of similar size in the neighboring undamaged areas. The walls of the venules in the injured area were lined with sheets of white cells all rolling along the inner surfaces of the endothelium (E. R. and E. L. Clark<sup>10</sup>). It seemed probable that this injured area would not form sludge much longer. 3. Normal, unagglutinated blood was coming from the uninjured areas.

At 7:30, three hours after the injury, these observations were noted: 1. The two venules originally thrombosed were still plugged up. 2. Patches of slightly agglutinated blood were forming at irregular intervals in blood flowing through the injured area. 3. Normal blood was coming out of the uninjured areas.

At 7:40 the same area was retraumatized by one light wiping stroke of the forceps handle. Immediately the blood flowing through the area became thick and pasty again. This shows that the substances which initiate sludge formation, or their precursors, were not all gone from the injured area.

At 7:55 p. m. the following observations were made: 1. Thrombosed vessels were still thrombosed. 2. Blood flowing through the injured area was still changing to a stiff sludge. 3. Normal blood was coming out of venules of neighboring uninjured muscle.

At 8:15 p. m. there was no change.

At 8:40 p. m. these observations were made: 1. Thrombosed vessels were still thrombosed. 2. All the blood flowing through the injured area was changing to a sludge and passing into the venous system. 3. Normal blood was coming from uninjured areas. The experiment was discontinued.

*Summary of This Experiment with Crushed Mouse Muscle.*—1. A light injury to mouse striated muscle caused precipitation and agglutination of the blood flowing through the injured area. Crush and flow through the crushed muscle were both necessary, and the two together were sufficient to produce a flow of sludged blood into the general circulation.

2. The precipitate was probably being formed in less than half a second.

3. For about one and three-fourths hours after the injury, the rate at which sludged blood was poured into the venous system was as fast as the rate of flow through the crushed area.

4. For the next one and one-fourth hours a progressively decreasing fraction of the blood flowing through this area changed consistency.

5. The clumps formed in the first period were fairly tough and rigid; those formed in the second period were increasingly plastic, flexible and fragile.

6. The visible sludge formed rapidly before the blood left the field being observed. This observation does not mean that all the sludge initiator substances reacted and became inactive within the microscope fields observed. Initiator substances which might be able to cause changes in the blood at some later time and distant place

may have been carried out of sight into the general circulation.

7. Retraumatization of the area reinitiated the formation of rather rigid clumps. This shows that the precursors of the initiator substances or the initiator substances themselves were not all gone from the area at the end of three hours, and it strongly suggests (a) that traumatized men should not be moved any more than necessary and (b) that when necessary to move them they should be moved as gently as possible to minimize the reinitiation of release of sludge initiator substances from previously traumatized tissues.

8. After retraumatization, the area poured sludged blood into the venous system for at least an hour.

9. The foregoing reactions occurred—hence can take place—in the absence of diapedesis of red cells or of hemorrhages or local hemoconcentrations and fluid loss at the sites of injury.

#### COMMENT

One experiment with crushed monkey omentum and one with crushed mouse striated muscle have now been described in detail.

In many other experiments on mice, larger single areas of striated muscle have been crushed and areas have been subjected to harder crushing, the most severe consisting in clamping a mosquito hemostat onto an area so tightly that on its removal the mashed muscle retained the impressions of the instrument's jaws and no blood flowed through the crushed area again.

The intestines of mice have also been crushed, sometimes lightly, sometimes more heavily. After all such injuries to the striated muscles and to the smooth muscle walls of the intestines of mice, three regions of each injury may be distinguished:

1. A region in which the small vessels are thrombosed. This region may be of any size, depending on the size of the instruments between which the tissue is traumatized and the force with which the tissue is crushed. This region pours no sludge into the venous system so long as its vessels are thrombosed.

2. A region at the side of or surrounding the first, a partially crushed region, in which the tissue is injured but through which blood is still flowing. This partially crushed region may be called the "sludging zone." Each small venule of this region pours sludged blood into the venous system.

3. A region at the side of or surrounding the partially crushed sludging zone in which the

tissues have not been injured enough to cause precipitation and agglutination of the blood flowing through them.

These regions are present in tissues which have been injured enough to cause transudation of plasma, diapedesis of red cells and hemorrhages (E. R. and E. L. Clark<sup>10</sup> and Phemister<sup>30</sup>), as well as in areas with lesser injuries.

Very slight injuries may have very small thrombosed zones. Heavier injuries have larger thrombosed regions. After delicate mouse muscle has been clamped with a strong hemostat and the hemostat then removed, the crushed and thrombosed zone is as large as the area of the jaw of the hemostat and the partially crushed sludging zone around it frequently is very narrow.<sup>37</sup> When a simple hard crush is made with a small hemispherical instrument, the thrombosed region is in or near the center of the crushed area, the sludging zone surrounds this and normal-appearing muscle containing normally flowing blood surrounds the sludging zone.

The edges of laparotomy incisions have been examined in many mice and in several rhesus monkeys. The sludging of blood passing in close proximity to the edges of laparotomy incisions can be seen wherever the tissues can be transilluminated and a microscope focused on the small vessels. All along each edge of each incision is a thrombosed zone. The cut and crimped ends of vessels are thrombosed. But where small vessels pass in close proximity to the injured tissue or through the injured tissue, the blood changes to a sludge as it passes through them. The tags of tissue at the edges of jagged laparotomy incisions often contain high proportions of partially crushed tissue.

When striated or smooth muscle is crushed with irregular objects or when multiple small crushes are made, thrombosed areas, partially crushed sludging zones and normal areas are all present, intermingled in various patterns. All the injuries we have studied have had each of the three zones. The degree of crush and the

36. Phemister, D. B.: The Mechanism and Management of Surgical Shock, *J. A. M. A.* 127: 1109 (April 28) 1945.

37. Advantage is now being taken of this fact in designing surgical technics for laboratory experiments. By using clamping and cutting procedures which keep the sludging zones very narrow, laparotomies can be performed in mice and monkeys without causing any microscopically detectable change in the consistency of the blood flowing through the eye vessels. So little sludge is produced that it does not appear in the general circulation in detectable amounts (Knisely, Stratman-Thomas, Eliot and Bloch<sup>6</sup> and Knisely, Bloch and Warner<sup>24</sup>).

pattern of the injury determine (a) the total volume of injured tissue and (b) the relative proportions of the thrombosed and partially crushed or sludged zones.

The amount of partially crushed tissue varies from injury to injury, but in each case it is the partially crushed tissue which pours sludge into the venous system. The amount of such partially crushed tissue present after an injury depends on the size and shape of the instrument, on the pressure applied and on the size and shape of the structures which supported the injured tissues.

From these observations, it seems probable that when they are crushed striated and smooth muscles release substances capable of diffusing in through the vessel walls and reacting with constituents of the blood flowing through the patent vessels.

From the observations it seems probable that the maximum amounts of initiator substances reach the blood from partly crushed tissue, that is, from regions injured enough to release the initiator substances but not injured enough to thrombose the enclosed vessels. The edge of a thrombosed region may of course be contributing initiator substances to a contiguous partly crushed region.

The sludge formed at the site of the injury is formed rapidly, before the blood leaves the field being observed, but this does not mean that all the sludge formed necessarily is formed at the site of the injury. Excess initiator substances which might be able to cause changes in the blood at some later time and distant place may well be being carried out of view into the general circulation. The observations reported thus far were made in mammals, but some observations made in amphibians (frogs and salamanders) may have a bearing on this point. In these animals an extensive operation done with care to prevent loss of blood (Kniseley, Bloch and Warner<sup>24</sup>), but without care to prevent partial crushing of tissues at the edges of incisions, is often followed by a slow increase in the viscosity of the plasma of all the circulating blood. In these animals a visible sludge may or may not form at the sites of injury. It seems reasonable to assume that in these amphibians initiator substances are carried into the general circulation before producing a visible change in the blood. Hence, by analogy it seems possible that in mammals excess initiator substances released at the sites of injury are being carried out of view into the general circulation. Such substances could cause further changes in the circulating blood and/or help bind masses of

sludge together into larger masses whenever they accumulate to or above some threshold concentration. This is not altogether an academic speculation; it may have a practical aspect, for transfusions given animals or men during or after the accumulation of such substances in the circulating blood must, among other things, dilute the initiator substances.

It seems reasonable to suspect that the initiator substances might be related to the substances capable of initiating blood clotting. If this is true, then sludge initiator substances should be released from many different injured tissues and organs of vertebrates.

The outer surfaces of the erythrocyte-containing masses formed in blood flowing through crushed tissues are not conspicuously different either in appearance or in observed behavior from the coated, red cell-containing masses formed in monkeys with *P. knowlesi* malaria. Hence, (a) the *P. knowlesi* malaria precipitates should be examined both chemically and immunologically to determine whether they are monkey fibrin or related to fibrin and (b) the precipitated coatings with their contained red cells formed in blood flowing through crushed tissues may be ingestible by phagocytes of spleen, bone marrow and liver. In monkeys with malaria, this mechanism destroys blood rapidly (Kniseley, Stratman-Thomas, Eliot and Bloch<sup>6</sup>). Thus the phagocytosis of coated red cells may well contribute to the removal of blood from the vascular system after a traumatizing injury and to the anemia which not infrequently follows operations (Kniseley, Bloch and Warner<sup>24</sup>).

A bit of sludge can reach the general circulation only by being carried into the venous system. Hence sludged blood can come from one minute injured area into the general circulation no faster than the flow through the venules which drain the injured area. These facts are important when one is considering the mechanisms of the crush syndrome (review and bibliography by Bywaters<sup>25</sup>).

The volume of sludge produced by the partially crushed area drained by one small venule may be expressed as the summation of volumetric rates of flow through the venule during the periods while sludge is produced. Hence, by induction, the amount of sludge produced by any partially crushed area is equal to the summation

38. Bywaters, E. L. G.: Ischemic Muscle Necrosis: Crushing Injury, Traumatic Edema, the Crush Syndrome, Traumatic Anuria, Compression Syndrome; a Type of Injury Seen in Air Raid Casualties Following Burial Beneath Debris, *J. A. M. A.* **124**:1103 (April 15) 1944.



of the amounts produced in each small venule of the area through which blood is flowing. Thus after injury the rate at which sludged blood is poured into the general circulation should be a result of (a) the volume of the partially crushed tissue and (b) the rates of flow of blood from the partially crushed area into the venous system. The total amount of sludge produced should be the result of these two factors and (c) the duration of the periods during which the sludge is produced by the injured area.

The amount of coated agglutinated blood cells (sludge) in the vascular system at any time must be equal to the amount produced up to that time minus the amount removed or destroyed or resolved into normal blood. More usefully expressed, the amount of sludge in the vascular system at any moment must be equal to the summations of the rates of production minus the summations of the rates of removal, destruction and disintegration up to that moment. Thus sludged blood should accumulate within the vascular system during the periods when the rates of production are greater than the rates of removal and resolution. If one injury or a group or series of injuries were large enough and the flow through their sludging zones fast enough, it should be possible to change all the circulating blood to a thick, mucklike sludge (Knisely and Bloch<sup>4b</sup>).

Microscopic studies are now an indispensable part of macroscopic studies of the circulatory system. At present it is not possible to determine with certainty by means of any known sign, symptom, blood pressure reading, kymograph record, sedimentation rate determination or other macroscopic indicator or by examination of histologic sections whether an experimental animal has, or has had, precipitated-agglutinated blood. Consequently, (a) it is not now possible to know that the blood was not precipitated and agglutinated to a circulating sludge in any previous experiment involving traumatic injuries and (b) it is not possible to carry out analytic experiments to determine the mechanisms operating in traumatic and other forms of shock or to determine the mechanisms operating in other experimental pathologic conditions without having continuous or closely spaced microscopic observations of the circulating blood as controls to determine whether and to what degree precipitation and agglutination of the blood is a part of the induced pathologic change. The "eye method" outlined in the methods section of this paper permits microscopic control of many types of gross physiology experiments.

The study of blood flowing past a minute local lesion may be useful for finding the sources of the substances which precipitate and agglutinate the blood in other pathologic conditions and diseases. Sludges, having various physical characteristics, have now been seen in human patients with diagnoses of about forty different pathologic conditions and diseases (Knisely and Bloch<sup>4</sup>). In each of these, the sources of the initiator substances must be found. Microscopic study of blood flowing past minute local lesions is one method of hunting for the sites of production of initiator substances. The technic should be used to study (a) small thermal burns, (b) small radium burns, (c) small roentgen ray burns, (d) small lesions caused by various chemicals, (e) small lesions of tuberculosis in experimental animals, (f) small areas inoculated through microneedles with various bacteria, (g) small neoplasms of all the kinds which can be obtained in experimental animals, (h) the sites of development of extraerythrocytic plasmodia in the malaras in which these occur and (i) the points of attachment of hookworms, trichina cysts, liver flukes and other parasites. New toxic substances or previously unknown effects of previously known toxins may be found (Youngner and Nungester<sup>39</sup>). The point is to get to the site of the lesion in vivo with adequate operative technics, light, temperature control and lenses.

#### SUMMARY AND CONCLUSIONS

For distribution of emphasis, the summary and conclusions is divided into sections on controls, methods and results of crushing injuries.

*I. Controls.*—1. The blood coming down the arterioles of each tissue is a statistically valid sample of all the flowing arterial blood in the body.

2. Most of the time, under most conditions, nearly all the circulating blood must, because of the anatomy and the dimensions of the living vascular system, pass through vessels having an internal diameter from about once to twice or at most three times that of the red cells on every trip around the circulatory system.

3. In normal animals and men the blood cells are not agglutinated, the red cells repel each other slightly and the white cells do not stick to vessel walls. The walls of capillaries, post-

39. Youngner, J. S., and Nungester, W. J.: Effect of Type III Pneumococcus Polysaccharide and Gelatin on Circulation and Sedimentation Rate of Erythrocytes in Mice, *J. Infect. Dis.* 74:247 (May-June) 1944.

capillary venules and venules do not leak enough to be detected by microscopic observation.

4. Pentobarbital sodium in anesthetic doses does not cause intravascular agglutination of the circulating blood of *Macacus rhesus* monkeys.

5. Neither pentobarbital sodium nor sodium amytal in anesthetic doses causes intravascular agglutination of the circulating blood of mice.

6. No single factor or combination of factors of the anesthetics used, the withdrawing of the monkey omentum or the brilliant transillumination of tissues whose temperatures are maintained at normal has caused intravascular agglutination of the blood.

7. Laparotomies can be done with sufficient care to prevent general precipitation and agglutination of all the circulating blood.

8. With routine care, normal monkeys have been kept under pentobarbital sodium anesthesia and the circulation in abdominal viscera observed with microscopes without causing general intravascular agglutination of the blood or visible pathologic changes in the walls of small blood vessels for as long as fourteen to eighteen hours.

*II. Methods.*—1. A method is described for maintaining controlled pentobarbital sodium anesthesia of monkeys by intrapleural injections; this is useful for making microscopic observations of abdominal structures.

2. Simple methods are described for studying the vessels and blood of the eyelid, nictitating membrane and bulbar conjunctiva of experimental animals not operated on and of those operated on. The methods have three obvious uses:

(a) To assist in preselecting normal animals for experiments. As agglutinated blood is not normal, as agglutinated blood has already been found as a part of the pathologic change in about forty human diseases and as many of the organisms which affect human beings also affect experimental animals, microscopic observations of the blood and vessel walls are a necessary part of the preselection of normal animals for experiments.

(b) To make continuous observations during the course of experiments on intact animals not operated on to determine the effects of various agents and procedures on the circulating blood and local vessel walls.

(c) To make continuous observations as controls to be certain that during experiments designed with the intention of studying normal animals no agent or procedure is causing mechanical changes in blood and/or pathologic changes in vessel walls.

3. A method is described for studying the blood passing through vessels in or near a minute local lesion. The method should be useful for studying the blood passing through or near lesions caused by many different agents.

*III. Results of Crushing Injuries.*—1. After a crushing injury to monkey omentum, smooth muscle of mouse intestine or striated muscle of a mouse, three zones may be distinguished: (a) a thrombosed zone, (b) a partially crushed or sludging zone and (c) a zone which is injured so little that the blood flowing through it undergoes no detectable change.

(Pentobarbital sodium in monkeys and mice and sodium amytal in mice do not in anesthetic doses prevent the precipitation-agglutination of blood flowing through a crushed area.)

Seen as possible initiating factors in traumatic shock, the observations made in these tissues may be summarized as follows:

2. Crushing plus flow through a vessel in the crushed area yields a stream of sludge into the general circulation.

3. Crushing plus thrombosis of a crushed vessel yields no sludge to the venous system.

4. Flow without crush yields no sludge.

5. Thus, after trauma, (a) local crush plus (b) flow through a vessel in the crushed area are both necessary and, together, sufficient to yield a flow of sludged blood into the general circulation.

6. After crush, precipitates can form around or between the moving blood cells in less than a second, while the blood is moving less than a millimeter.

7. It seems reasonable to suspect that the sludge initiator substances might be related to the substances capable of initiating blood clotting. If this is true, then many tissues and organs of vertebrates should release such substances when they are injured.

8. At no time can sludged blood pass into the venous system faster than the flow through the crushed tissue.

9. For a time after the crush, the rate at which sludge is poured into the venous system can be as fast as the rate of flow through an open vessel in the crushed area.

10. Retraumatization of an area can reinstate sludge formation in blood flowing through the area.

11. This sludge can be formed in an area from which or into which there is (a) no hemorrhage and (b) but little loss of plasma through injured vessel walls.

12. This sludge is also formed in the partially crushed regions of areas injured severely enough to cause local transudation of plasma, diapedesis of red cells and/or hemorrhages through walls of injured local vessels.

13. When first formed, some of the masses have sufficient internal rigidity to bulge the walls of the vessel through which they are being forced; if not changed, such masses would resist passage through capillaries.

14. When first formed, the outer surfaces of the precipitated material is sticky to itself; hence, if not changed, such masses must, whenever they touch each other, tend to stick together and form larger masses.

15. The outer surfaces of the red cell-containing masses formed in blood flowing through crushed tissues are not visibly different in appearance or in observed behavior from the coated red cell masses formed in monkeys with *P. knowlesi* malaria.

16. Hence, the precipitated coatings with contained red cells formed in blood flowing through

crushed tissues may be ingestible by phagocytes of spleen, bone marrow and liver. In monkeys with malaria, this mechanism destroys blood rapidly.

17. During periods when the rates of production of sludge are faster than the rates of removal and/or the resolution of sludge, sludged blood should accumulate under the vascular system. If one injury or a group or a series of injuries were large enough and the flow through their sludging zones fast enough, all the circulating blood should should change to a thick, mucklike sludge.

One of our problems consists in attempting to present material which can be recorded only in motion pictures in conventional published form. A single frame from a motion picture seldom contains sharp enough detail for publication as a still picture, and no still photograph records or gives the impression of continuous processes. The figure in this paper was designed to retain in sharp accuracy the dimensions of the living stationary structures and, in addition, give an impression of the rapid movement of the vessel contents. The figure was made by Dock Curtis, artist and medical student, amid a general feeling that it could not be done.

# A NEW TREATMENT FOR POSTOPERATIVE PULMONARY COLLAPSE

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Of all the complications following surgical procedures, those involving the lungs are among the most feared and the most commonly reported.<sup>1</sup> The incidence of atelectasis has been variously reported as causing from 3 to 70 per cent of all postoperative complications, with 40 per cent mortality among the persons affected.<sup>2</sup> In operations of the upper part of the abdomen the morbidity from respiratory complications is said to be about 10 per cent.<sup>2</sup> At the Kansas City Gen-

eral Hospital during two years in which careful records have been kept, the incidence of morbidity and mortality from respiratory complications is seen to be much lower (tables 1 and 2).<sup>3</sup> All patients with atelectasis and massive pulmonary collapse in this series recovered speedily. Pneumonia was named as the cause of death or was associated with other causes in 24 of 125 postoperative deaths. In most cases the pneumonia occurred as a terminal process a number of days following operation and was associated

TABLE 1.—Results in Cases in Which Anesthetic Was Used

	Number of Cases	Respiratory Complications, Number of Cases			Respiratory Complications, %	Mortality, Number of Cases			Respiratory Complications, %		
		Collapse	Atelectasis	Pneumonia		Collapse	Atelectasis	Pneumonia	Collapse	Atelectasis	Pneumonia
Spinal.....	718	2	7	14	3.1	0	0	0	0.28	0.9	1.8
Cyclopropane.....	816	0	2	13	1.6	0	0	1	0	0.27	1.6
Ether (open drop).....	275	2	3	5	3.2	0	0	1	0.73	1.09	1.8
Nitrous oxide-ether.....	19	1	0	10	57.9	0	0	2	5.2	0	52.6
Cyclopropane-ether.....	100	2	3	3	8.0	0	0	1	2.0	3	3
Nitrous oxide.....	136	0	0	3	2.3	0	0	2	0	0	2.3
Pentothal sodium.....	538	0	0	0	0	0	0	0	0	0	0
Spinal-gas.....	102	0	0	3	3.0	0	0	3	0	0	3.0
Total.....	2,704	6	15	51	2.6	0	0	24	0.22	0.55	1.8

To summarize this table, in 0.22 per cent of all cases in which an anesthetic was used there was massive collapse of the lungs; in 0.55 per cent atelectasis and in 1.8 per cent pneumonia, with an ultimate mortality of 0.88 per cent for all cases in which an anesthetic was used (33 per cent of the total morbidity from disease of the respiratory tract.)

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TABLE 2.—Percentage of All Cases Having Post-operative Complications

	Drop Ether, %	Cyclopropane, %	Spinal, %	Nitrous Oxide, %	Pentothol Sodium, %
Nausea and emesis.....	47	28	17	15	11
Distention.....	8	8	10.9	2	0
Catheterization and retention.....	21	14	15	18	4
Tachycardia.....	32	18	20.5	11	5.5
Pneumonia.....	1.8	1.7	2.0	2.0	0
Atelectasis.....	1.09	0.27	0.9	0	0
Massive collapse.....	0.73	0	0.28	0	0
Fall in blood pressure without shock.....	3.5	3.4	1.0	4.0	0
Shock.....	5.0	1.4	2.0	0	0
Headache.....	5.0	6.0	5.7	0	2.2
Other complications, as wound infection, neuritis, cough, irrational, embolism, etc.....	5.0	10.0	25.7	3	5.2

Read before the Kansas City Academy of Anesthesiology, Kansas City, Mo., May 2, 1945.

1. Adams, W. E.: Thoracic Surgery: Postoperative Pulmonary Atelectasis, *Am. J. Surg.* 56:180-191 (April) 1942.

2. Elkin, D. C.: Postoperative Pulmonary Complications, *Surg., Gynec. & Obst.* 70:491-493 (Feb.) 1940.

3. Grandstaff, E. H., and Schaerrer, W. C.: Progress in the Anesthetic Department of the Kansas City General Hospital, 1940, *J. Missouri M. A.* 38:352-353 (Oct.) 1941.

tive complications of all types.<sup>3</sup> the high percentage of oxygen which it is possible to give during the administration of the anesthetic and the lack of injury to the liver or kidneys or of other pathologic damage. Many of these patients

already had nephritis, peritonitis, pathologic conditions of the lung or cardiac decompensation, and the morbidity and mortality from respiratory complications in these cases cannot be considered as primarily due to the anesthetic agent. At the other extreme, ether is not given at this hospital, exclusive of operations on ear, nose and throat, except to patients who are in excellent condition. The more frequent respiratory complications following the use of ether, either by itself or in combination with one of the gases, are thus due directly to the anesthetic agent, because of its irritating effect on the lung tissue, with stimulation of bronchial secretions, production of a high percentage of nausea and vomiting, with attendant danger of aspiration, and a long recovery period with depressed respiration.

There have been many suggestions as to the cause of postoperative collapse.<sup>4</sup> It is most likely to occur after operations high in the abdomen from splinting of the lower intercostal muscles or from pain, resulting in diminished aeration, and stagnation of mucous secretions.<sup>5</sup> Pain from the incision in operations on the abdomen has been found to cause a 59 per cent depression of vital capacity by a reflex inhibition of respiration.<sup>6</sup> When following operation on a kidney, the collapse and atelectasis always occur on the opposite side from the operative site, probably because of interference with respirations by the elevation of the kidney rest and by accumulation of secretions on the dependent side. This is the case in the present series, with massive collapse of the left lung on the third day following a nephrectomy on the right side (case 1).

Any patient with severe oral sepsis, chronic bronchitis or acute or chronic infection of the respiratory tract should be regarded as a possible candidate for postoperative collapse and given special treatment to attempt to prevent it.<sup>1</sup> Most of the patients in this series who had a severe degree of pulmonary collapse had a pronounced oral sepsis.

Excessive postoperative sedation should be avoided, as this raises the threshold of stimula-

4. (a) McCall, J. W., and Freeman, M. S.: Postoperative Atelectasis: Presentation of Four Cases, *Ohio State M. J.* 38:546-550 (June) 1942. (b) Moore, A. E.: The Treatment of Postoperative Pulmonary Atelectasis, *Surgery* 5:420-435 (March) 1939. (c) Gius, J. A.: Postoperative Atelectasis and Related Pulmonary Complications: Collective Review, *Internat. Abstr. Surg.* 71:65-78, 1940; in *Surg., Gynec. & Obst.*, July 1940. (d) Adams.<sup>1</sup>

5. Marshall, J. M.: Postoperative Pulmonary Atelectasis, *U. S. Nav. M. Bull.* 42:601-606 (March) 1944.

6. Collier, F. A., and Singleton, A. O.: Postoperative Complications, *South. Surgeon* 11:560-573 (Aug.) 1942.

tion of the cough reflex by accumulated secretions. Atropine or scopolamine should not be administered postoperatively, as it merely inspissates the mucous secretion and prevents the patient from coughing it up. A tight binder or severe abdominal or bladder distention will reduce the vital capacity and allow stagnation and accumulation of secretions. Preoperative sedation should not be excessive, as this, together with the use of cyclopropane, will seriously depress the respiration and allow congestion and accumulation of secretions during a long operation under deep anesthesia. Atropine and scopolamine should not be given immediately preceding the anesthetic, but there should be an interval of about forty-five minutes, at the end of which time these drugs reach their maximum anhidrotic effect. If given and followed immediately by the anesthetic, an excess of mucus will be formed owing to the effect of the anesthetic before the drugs have had time to reach their full effectiveness. Then later this mucus which has been formed during the first few minutes of the anesthetic will be dried and remain in the bronchioles as a plug.<sup>4a</sup> This is well illustrated by case 3, in which scopolamine was administered and the cyclopropane-ether anesthetic started immediately, the preceding operation having been canceled and the surgeon being in an uncooperative mood and stating that it made no difference when the premedication was given. Massive collapse of the lung followed twenty-three hours later.

The type of anesthetic appears to have more significance in this series than is usually attributed to it. Pulmonary complications followed 3.2 per cent of the inductions of anesthesia with ether by the open drop method. Complications following 3.1 per cent of the inductions of spinal anesthesia may be due to the paralysis of the lower intercostal muscles in the case of high spinal anesthesia.<sup>5</sup> However, in this series, complications occurred just as frequently after the use of low spinal anesthesia. Postoperative position, especially for old people, is considered as more contributory than the average spinal anesthetic, as the paralysis of the intercostal muscle produced by spinal anesthesia is worn away within four hours, except after use of nupercaine hydrochloride or continuous spinal anesthesia.<sup>5</sup>

Most interesting is the finding that ether combined with oxygen following induction of anesthesia by nitrous oxide or cyclopropane produces a prohibitively high percentage of respiratory complications. This is due to the great irritation by the ether of the bronchial mucosa, causing

mucus and obstruction; the high percentage of oxygen in this inspired closed ether atmosphere allows its almost immediate removal by the blood stream, leaving a collapsed lung behind one or numerous small obstructive masses of mucus.

Cyclopropane was followed by the fewest pulmonary complications as well as other types of complications, in spite of the fact that it is administered to those patients already extremely ill but requiring operation. It causes a negligible amount of bronchial irritation and production of mucus. In a few cases collapse follows administration of cyclopropane, particularly when combined with a large dose of morphine, because of the depression of the respiration from the removal of the carbon dioxide to produce purposely a shallow respiration and a quiet abdomen for surgical intervention.

Aspiration of blood or vomitus during or after operation is an important consideration also, as this may plug the bronchioles. If the airway does not seem to be perfectly clear at the end of operation, this aspiration should be done before the patient is removed to the ward.

The onset of pulmonary collapse occurs suddenly, usually during the first three days, with pain in the chest, dyspnea and a sharp rise in temperature and in pulse and respiration rates. The patient is usually found sitting up in bed, anxious, dyspneic and cyanotic. There is more or less fixation of the affected side, with dullness on percussion, absence of breath sounds, elevation of the diaphragm and shift of the area of cardiac dullness toward the affected side. The unaffected side is hyperresonant, and there are increased breath sounds.<sup>4a</sup> The sputum is scanty at first but quickly becomes abundant and mucopurulent. The white blood cell count may be 15,000 to 20,000. The roentgenogram is characteristic, with elevation of the diaphragm on the affected side, narrowing of the intercostal spaces and deviation of the heart and other mediastinal structures to the affected side, the lung appearing dense and homogenous.

Treatment of such collapse is, of course, primarily prophylactic. As soon as the operative schedule is posted for the following day, the intern on the anesthesia service and I examine each patient and plan the type of anesthetic which will be the best, considering the pathologic condition of the patient, the type of operation proposed and the use of cautery or roentgen ray equipment. A member of the anesthesia department then writes orders for the preoperative medication, giving a small dose of morphine for all patients except those who are young and vigorous. By small dose is meant  $\frac{1}{16}$  grain

(0.0037 Gm.) to  $\frac{1}{8}$  grain (0.007 Gm.) for those above 50 years,  $\frac{1}{8}$  grain to  $\frac{1}{6}$  grain (0.01 Gm.) for those from 50 to about 25 years and  $\frac{1}{6}$  grain for those in good condition, in their twenties and thirties. Occasionally  $\frac{1}{4}$  grain (0.015 Gm.) is given in this group. Scopolamine is given in combination with the morphine preceding spinal anesthesia for further sedation,  $\frac{1}{150}$  grain (0.0004 Gm.) to  $\frac{1}{300}$  grain (0.0002 Gm.) being given with increasing age. Atropine is given preceding an anesthetic administered intravenously, as it has been found that there is more likely to be a fall in blood pressure during the administration of pentothal sodium if it has been preceded by the use of scopolamine. Atropine is also given to young children in preference to scopolamine, which rather seriously depresses them. Administration of the anesthetic is refused until the patient has received atropine or scopolamine for the proper interval previous to operation. Barbiturates are given to all patients preceding use of caudal, epidural or spinal anesthesia to avoid procaine reactions through depression of the central nervous system from stimulation of procaine and its derivatives. Barbiturates are given to those patients to receive nitrous oxide anesthesia to depress the metabolism further, which is necessary when administering this weak gas. They are also given preceding use of cyclopropane to decrease vagal tone and prevent cardiac arrhythmia from the combination of morphine and cyclopropane.<sup>7</sup> Ortol sodium is given to older people, over 50, and pentobarbital sodium in one or two 1.5 grain (0.009 Gm.) doses to younger patients. Seconal when combined with even a small dose of scopolamine has been found to be too depressing to the respirations of old people. Morphine and barbiturates are not given preceding tribromoethanol, as this combination produces severe respiratory depression. At the close of the anesthesia, an attempt is made to have the patient partially awake and to have his pharyngeal reflex back. Nitrous oxide is given during the last few minutes of cyclopropane anesthesia in order to fill the lungs with a substance which is much more slowly absorbed in case a portion of the lung should be cut off behind a mucus plug. Nitrous oxide requires several hours to be dissolved by the blood stream, while cyclopropane and oxygen are removed in a few minutes and in that case would leave a portion of lung collapsed in a short time. I have not seen a case of atelectasis develop after this

7. Robbins, B. H.; Baxter, J. H., and Fitzhugh, O. G.: The Use of Barbiturates in Preventing Cardiac Irregularities Under Cyclopropane or Morphine and Cyclopropane Anesthesia, *Ann. Surg.* **110**:84-93 (July) 1939.

precaution, even when operation is done high in the abdomen. Use of one of the elastic adhesives has been found useful in dressing wounds high in the abdomen snugly and yet allowing expansion of the chest.

When the patient is removed to the ward, he is placed at once on the side opposite to that on which he has been operated, the theory being that if the lung on the opposite side is constricted slightly by his weight there will be a compensatory expansion of the lung on the operated side and stimulation of deeper respiration with not so much splinting of the chest. After this, the position is changed from one side to the other every hour<sup>4b</sup> when the patient is not receiving intravenous infusions. No patient is to be placed in bed on his back and left there quietly indefinitely. The first day, inhalations of carbon dioxide and oxygen are given for two minutes out of every hour and the second day out of every two hours. The patients are then urged to take ten deep breaths voluntarily every hour. Postoperative sedation is held at a minimum, and no atropine or scopolamine is given. Because these measures have been followed, there has not been a case of massive collapse at this hospital in two years and only a few cases of mild atelectasis, which cleared up promptly with little special treatment.

If, in spite of these precautions, pulmonary atelectasis or collapse develops, the patient should be placed on the unaffected side in a moderate Trendelenburg position. He should be instructed to cough, with some one holding his abdomen, if the condition follows an operation on the abdomen, to give support to the abdominal wall and decrease the pain of coughing. A tight scultetus binder may be used to give abdominal support for a short time. Striking the patient on the back over the affected lung while encouraging him to cough will often help to dislodge the plug.<sup>4b</sup>

A new treatment consisting merely in cocaineizing the throat with 5 to 10 per cent cocaine solution has been used in a number of cases, with spectacular results and almost instant cure in many cases (see cases 4 and 5 for roentgen demonstration). The cocaine solution in a cotton ball held in a curved applicator is placed far back in the throat and into the pyriform sinuses as if in preparation for a bronchoscopy. It has been found that the use of this procedure apparently relaxes the musculature of the bronchial tree enough that within a few minutes the patient will cough up a large plug of mucus and be relieved at once. Use of a little solution of epinephrine in the same cotton pledget will help stimulate the cough reflex. The patient is en-

couraged to cough, with some one giving support to the abdomen. This relaxing effect from the cocaine is thought to be the essential part of the procedure. Merely applying a cotton ball moistened with isotonic solution of sodium chloride or solution of epinephrine by itself to the back of the throat to produce hard coughing will not produce the desired effect. Application of the cocaine is followed by expulsion of the obstructing plug and dramatic relief in many cases.

During the next twenty-four hours or more, use of intermittent inhalation of oxygen and carbon dioxide is continued, to keep respirations deep and to attempt to reexpand all bronchioles. Chemotherapy with sulfathiazole or sulfadiazine is begun and continued for twenty-four hours or longer to prevent pneumonia from beginning in the congested and airless area.<sup>1</sup> The patient is rolled from one side to another frequently and made to continue to cough and take deep breaths. A set of blow bottles has been devised so that the patient can blow the water from one bottle into the other every hour; this helps increase and maintain expansion of the lung tissue.

There have been no failures from use of this method of cure of pulmonary collapse merely by cocaineization of the throat. It has not been necessary in this hospital to resort to use of bronchoscopy, with its production of additional strain on the abdominal incision and great discomfort of the patient, since we have been using these measures.

#### REPORT OF CASES

CASE 1.—M. H., a fairly well nourished woman 33 years old, was brought to surgery October 31 for a nephrectomy on the right side on account of a complaint of severe pain in the right side and back, with discovery on the intravenous pyelogram of a large branching calculus in the right renal pelvis. Other history is noncontributory except for a chronic cough, and physical examination showed nothing significant. Phenol-sulfonphthalein was excreted at a rate of 12.5 per cent on the right side and 37.5 per cent on the left side in two hours. The urine was loaded with white blood cells, with a heavy trace of albumin. Wassermann and Kahn tests of the blood elicited negative reactions. The sugar content was 88 mg., the nonprotein nitrogen level 28.5 mg. and the creatinine content 1.5 mg. per hundred cubic centimeters. The hemoglobin content was 10 per cent and the white blood cell count 6,600. The sedimentation rate was 17 mm. A mixture of 75 mg. of procaine hydrochloride crystals and 12 mg. of tetracaine hydrochloride in solution were administered in the first lumbar space; removal of a large rough kidney was accomplished without incident in an operation lasting sixty-six minutes, and the patient was returned to the ward in good condition. On November 1, terpin hydrate with codeine was given for the cough, with ammonium chloride and continuous inhalations of steam. Morphine,  $\frac{1}{4}$  grain (0.015 Gm.), was given only once. On November 2 (Sunday) the patient was complaining of dysp-

nea and expectorating gray sputum. Some distention was present. Her temperature was 102.2 F. Codeine was given for relief of pain. November 3 the chest was examined roentgenologically, and the condition of the patient was reported to the anesthesia department. She was found dyspneic and anxious and cyanotic and she was coughing and retching almost continuously. The temperature was 102.2 F. and the pulse rate 120. Roentgen ray examination showed diffuse clouding of the entire left lung, and the central shadows were displaced toward this side, with increased aeration on the right. Cocainization of the larynx was done, with expectoration in a few minutes of a large mucus plug and large amounts of purulent mucus. A roentgenogram taken at once showed partial clearing of the left pulmonary field with progressive clearing November 4 and 5. Inhalations of carbon dioxide and oxygen were started and also chemotherapy with sulfathiazole; blowing up of blow bottles was instituted, with relief of the collapse, though a pulmonic process in the base of the left lung persisted until November 17.

This case illustrates the necessity for recognition and treatment of a condition of collapse at once before pneumonia begins, which happens speedily in a congested and airless area of lung and which prolongs the recovery period a number of days.

CASE 2.—E. D., a poorly nourished white man 48 years old, was brought to surgery on July 15 for repair of a recurrent inguinal hernia on the left side, which had been repaired eight years ago. His history was noncontributory except for the fact that he smoked excessively and had a chronic nonproductive cough. Physical examination revealed carious teeth with spongy, receding gums and a moderately injected pharynx. A few moist rales were heard in the left axilla. Twelve milligrams of pontocaine hydrochloride solution was given in the second lumbar space; the hernia was repaired without incident in fifty-five minutes, and the patient was returned to the ward in good condition. Inhalations of carbon dioxide and oxygen were refused, and the patient refused to take deep breaths or to cough. A roentgenogram was taken July 16 on account of pleuritic pain in the right base of the chest, with a friction rub; it revealed clouding of the base of the right lung with elevation of the diaphragm, and was interpreted by the roentgen ray department as "suggestive of pleurisy." The temperature at this time was 99.8 F. Morphine sulfate,  $\frac{1}{2}$  grain [0.01 Gm.], was being given three times a day. His temperature rose to 102.6 F. on July 17, and he had severe pain in the back. Administration of sulfathiazole was begun, with rapid improvement. The temperature was 99 F. On July 19 another roentgenogram was taken on account of increased pain, which revealed a large shadow above the right side of the diaphragm with a shift of the trachea to the right. The throat was cocainized with 10 per cent cocaine solution, and the patient coughed up a large mucus plug and stated that the pain was less intense. He remained comfortable, and his condition steadily improved. Use of sulfathiazole together with ammonium sulfate was continued for forty-eight hours with no further incident.

CASE 3.—N. G., a poorly nourished woman 27 years old, was brought to surgery on June 19 for suspension and perineorrhaphy. The history revealed chronic pelvic inflammatory disease, with recent septic abortion with hemorrhage. The hemoglobin content was 81 per cent, the sugar content 104 mg., the nonprotein nitrogen level

27.9 mg. and the creatinine content 1.4 mg. per hundred cubic centimeters. The operation preceding this one had been canceled, and so the patient was brought to the operating room and premedication of seconal, 3 grains (0.19 Gm.), given at 7:30 a. m., morphine sulfate  $\frac{1}{6}$  grain (0.01 Gm.), and scopolamine hydrobromide  $\frac{1}{200}$  grain (0.0003 Gm.), being given at the same time. Administration of cyclopropane was begun at 7:42 a. m., followed by closed ether. The surgeon had insisted that the anesthetic be begun immediately, stating that it made no difference when the premedication was given. A dilation and curettage, perineorrhaphy, trachelorrhaphy and Gilliam's suspension were done during the next hour and thirty minutes, and the patient was returned to the ward in good condition at 9:50 a. m. At 10:30 a. m. on June 20 she was seized with sudden pain in the right side of the chest, with dyspnea, anxiety and tachycardia. Examination revealed the right side of the chest unexpansive on respiration, an absence of breath sounds in the right base and coarse rales heard in the right apex. Roentgen ray examination showed massive collapse of the right lung, with the mediastinum and trachea shifted to the right. Cocainization of the throat was done within half an hour and coughing encouraged. A large hard mucus plug was expectorated, with the patient experiencing great relief of dyspnea and anxiety. The cyanosis improved almost at once. Roentgen ray examination showed partial clearing of the chest. Inhalations of carbon dioxide and oxygen and blowing up of blow bottles were started. By 4 p. m. the roentgenogram revealed the right side of the chest nearly clear, with the diaphragm returned to a normal level. Sulfathiazole was discontinued June 21, and the patient remained free from further symptoms.

CASE 4.—R. O., a poorly nourished woman 43 years old, was brought to surgery March 18 for exploratory laparotomy on account of large pelvic masses. She had been bleeding profusely for four months, with a hemoglobin content on her admission to the hospital (February 26) of 27 per cent. The rest of the history was noncontributory, and physical examination at this time revealed exceedingly carious teeth and spongy gums and a soft blowing mitral systolic murmur disappearing on exercise. Hemoglobin content at the time of operation was 65 per cent, the sugar content 108 mg., the nonprotein nitrogen level 31.6 mg. and the creatinine level 1.7 mg. per hundred cubic centimeters. The urine test revealed nothing abnormal. Premedication of morphine,  $\frac{1}{6}$  grain (0.01 Gm.), and scopolamine hydrobromide,  $\frac{1}{200}$  grain (0.0003 Gm.), was given and fifty-five minutes later drop ether was begun, as the surgeon insisted that ether be used for all of his patients. Bilateral salpingo-oophorectomy was done during a one hour operation without incident, and the patient was returned to the ward in good condition at 10:30 a. m. Her condition remained good until March 19 at 8 p. m., when she complained of shortness of breath and pain in the right side of the chest. The temperature was 102.8 F. and the pulse rate 160. There was an absence of breath sounds in the right side and hyperresonance in the left side of the chest. The medical service was consulted and gave advice to treat the patient as for pneumonia. Administration of sulfapyridine was started, but by morning the patient was worse and symptoms were more pronounced. A roentgenogram taken during the morning revealed a complete collapse of the right side of the chest (fig. 1.4). At 2:15 p. m. the anesthesia department was consulted, and the throat was cocainized at once with 10 per cent cocaine. During the procedure the patient was thrown into a paroxysm of coughing that resulted in the expectoration of copious quantities



of mucopurulent material; breathing immediately became easier, and breath sounds began to be heard over the right side of the chest. Check roentgenograms one and one-half hours later revealed reexpansion of the right lung, with change of the heart shadow to a more nearly normal position (fig. 1 *B*). Inhalations of carbon dioxide and oxygen every half hour were begun, blow bottles were blown up every hour and administration of sulfapyridine was continued. Roentgenograms

CASE 5.—N. S., a well nourished woman 43 years old was brought to surgery January 22 for exploratory laparotomy for abdominal pain and hyperesthesia of the abdominal wall. Bilateral salpingectomy, oophorectomy on the left side and supravaginal hysterectomy had been done nine months previously. Severe pain at the upper end of the incision intermittently since this operation was the chief complaint. The other history was noncontributory. Physical examination revealed

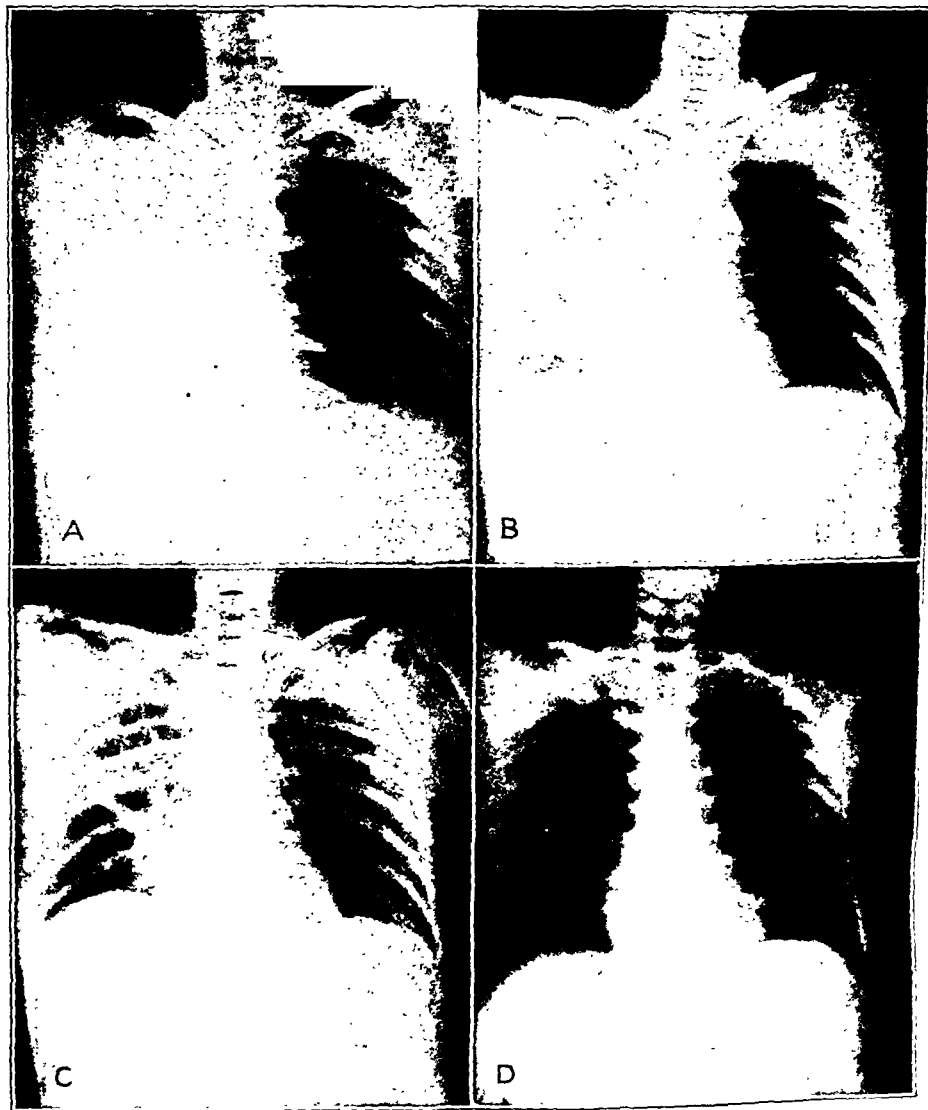


Fig. 1 (case 4).—*A*, immediately before treatment showing complete collapse of the right lung, with shifting of the tracheal shadow and the heart shadow to the right. *B*, one and one-half hours after cocaineization of throat and expectoration of large quantities of mucus, showing partial reexpansion of right lung. *C*, on morning following cocaineization of throat, showing almost complete reexpansion of right lung and shifting of tracheal shadow to normal position. *D*, three days after treatment for collapse, showing complete restoration and clearing of lung.

on March 21 revealed an almost complete reexpansion of the lung, with return of the tracheal shadow to the normal medial position (fig. 1 *C*). Three days later roentgenograms showed complete clearing of the lung, with return of a normal temperature (fig. 1 *D*).

no abnormalities other than extremely carious teeth. Pentobarbital sodium,  $1\frac{1}{2}$  grains (0.09 Gm.), was given at 8 a. m., and morphine sulfate,  $\frac{1}{8}$  grain (0.007 Gm.), and scopolamine,  $1/200$  grain (0.0005 Gm.), were given at 10:10. Nitrous oxide, 92.8 per cent, was begun

at 10:30 a. m., followed by closed ether anesthesia for maintenance. Lysis of extensive adhesions of the omentum into the pelvis was done. The operation lasted an hour and fifty-three minutes, and the patient was returned to the ward in good condition at 12:50 p. m.

sulfate and sulfapyridine. Copious expectoration resulted from cocainization of the throat, with pronounced relief experienced by the patient. A roentgen ray examination at 8 a. m. revealed two-thirds clearing of the left base, with still a slight shift of the mediastinal

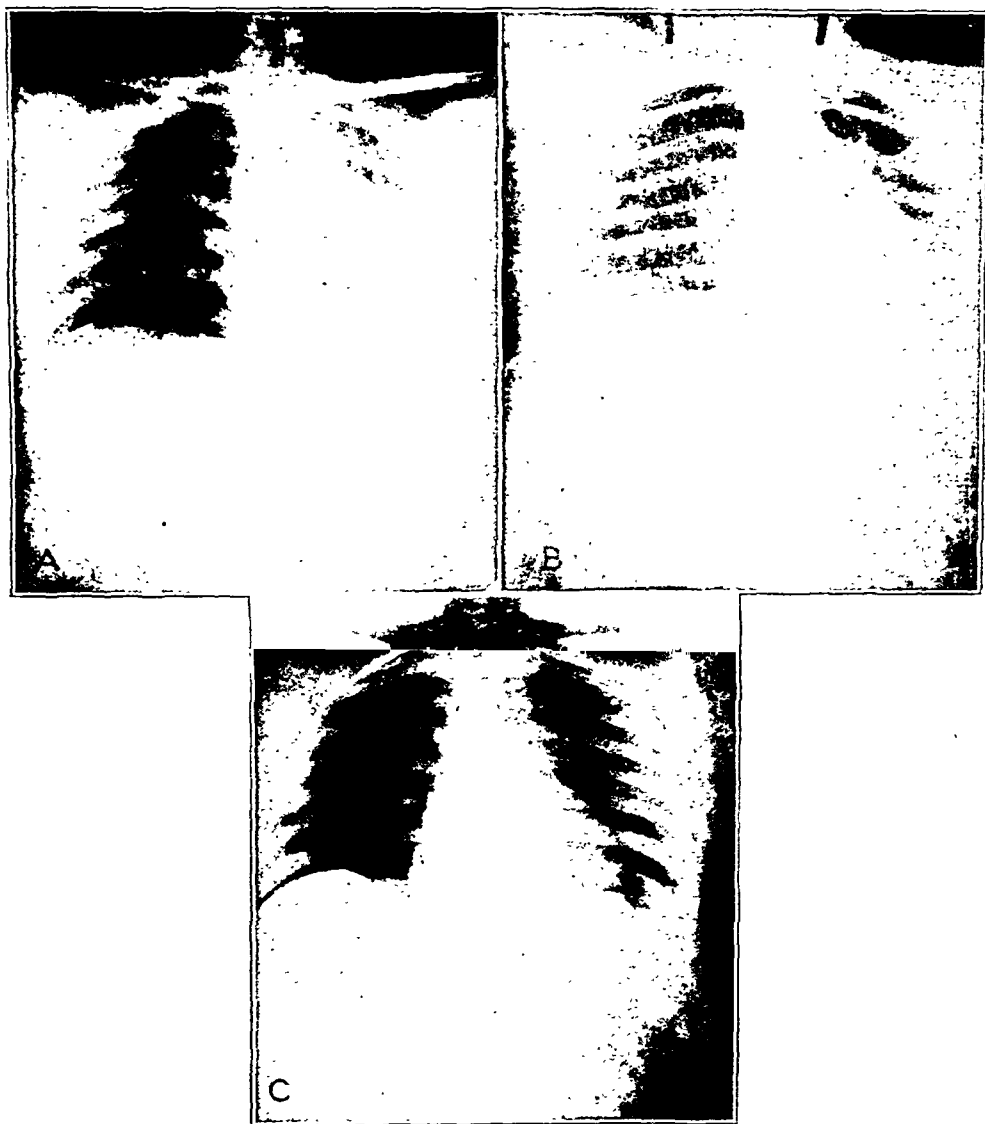


Fig. 2 (case 5).—*A*, showing collapse of the lower lobe of the left lung before treatment. *B*, showing reexpansion of the left base shortly after treatment and two hours after initial collapse. *C*, showing complete reexpansion and clearing of the left lung ten hours after initial collapse, with immediate treatment.

She was talking at 1:50 p. m. At 6 a. m. January 23, she was found cyanotic and complaining of pain in the chest. A roentgenogram revealed collapse of the left lung (fig. 2*A*). Swabbing of the throat with epinephrine and cocaine was started, with inhalations of carbon dioxide and oxygen and use of ammonium

shadow (fig. 2*B*). Roentgen ray examination at 4 p. m. showed complete clearing of the base of the left lung (fig. 2*C*).

This case also illustrates the value of immediate treatment in preventing pneumonia following collapse of the lung.

# ELECTROLYTE CHANGES AND CHEMOTHERAPY IN EXPERIMENTAL BURN AND TRAUMATIC SHOCK AND HEMORRHAGE

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During the past few years, observations have been made on experimentally produced burn and traumatic shock and death from hemorrhage in over 10,000 small laboratory animals. This report of our results is being made because of their possible significance in clinical practice.

Knowledge of the circulatory disturbances in shock has recently been greatly enlarged, but the nature of the underlying mechanisms has remained obscure. For this reason the therapy of shock has been directed primarily toward correction of these demonstrable alterations in the circulation, perhaps to the neglect of important changes in the tissues.

In the field of therapy, a review of the literature reveals a diversity of results from laboratory investigation.<sup>1</sup> This is an expression of the difficulties encountered in the standardization of methods and, to some extent, of the fact that with large laboratory animals it is difficult to employ adequate numbers to compensate for wide biological variations.

In order to obtain standardized and reproducible conditions, simplified methods were developed by which mice or rats could be used. These methods permit the use of a hundred or more animals in a single day's experiment, and with mortality as a basis of comparison it is possible to evaluate therapeutic procedures under uniform conditions.

Burn shock was produced by immersion to the axilla of the shaved etherized animal in water at 70 C.<sup>2</sup> Traumatic shock was produced by

placing tourniquets (rubber bands) on the hind-legs of etherized animals for two or more hours. Anesthesia was employed only during the brief period of application of the trauma. Hemorrhage was carried out by placing the cut tails in measuring cylinders containing warm oxalate solution. Bleeding was produced in two stages, with a one hour intermission between bleedings; the first bleeding amounted to 2.25 per cent of the body weight, and the second bleeding was continued until the death of a high percentage of the untreated animals (4.5 to 5 per cent body weight). The quantity of blood loss required to produce death was taken as a basis of comparison.<sup>4</sup> All forms of trauma were so standardized that the average mortality among control (untreated) animals within forty-eight hours was greater than 90 per cent.

## FLUID AND ELECTROLYTE CHANGES IN TRAUMATIC SHOCK

Tourniquet shock was chosen for these experiments because it is possible to amputate the injured tissues (legs) and determine the changes which occur in the entire injured area. Control analyses on groups of normal animals kept under the same conditions and carried out at the same time served as a basis for comparison. This technic has been found valid when pooled samples from groups of 5 or more animals are used.

The results<sup>2</sup> of these analyses demonstrate that the local accumulation of fluid in untreated mice two hours after the injury amounts to

From the Division of Physiology, National Institute of Health, United States Public Health Service.

1. Adequate references to the large literature are not possible in this paper. The following reviews may be consulted: Harkins, H. N.: Recent Advances in the Study and Management of Traumatic Shock, *Surgery* 9:231 (Feb.); 447 (March); 607 (April) 1941. Blalock, A.: Principles of Surgical Care, Shock and Other Problems, St. Louis, C. V. Mosby Company, 1940. Moon, V. N.: Shock: Its Dynamics, Occurrence, and Management, Philadelphia, Lea & Febiger, 1942. More recent references may be found in the papers cited below.

2. Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock: (a) I. Methods; II. Effects of Local Therapy upon Mortality from Shock, *Pub. Health Rep.* 57:1923-1935 (Dec. 18) 1942; (b) III. Effects of Systemic Therapy on Early Mortality, *ibid.* 58:513-522 (March 26) 1943.

3. Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock: IV. Production of Traumatic Shock in Mice; V. Therapy with Mouse Serum and Sodium Salts, *Pub. Health Rep.* 58:1429-1438 (Sept. 24) 1943.

4. Tabor, H.; Kabat, H., and Rosenthal, S. M.: The Chemotherapy of Burns and Shock: VI. Standardized Hemorrhage in the Mouse; VII. Therapy of Experimental Hemorrhage, *Pub. Health Rep.* 59:637-643 (May 19) 1944.

5. Tabor, H., and Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock: VIII. Effects of Potassium Administration, of Sodium Loss, and Fluid Loss in Tourniquet Shock, *Pub. Health Rep.* 60:373-380 (April 6) 1945; Electrolyte Changes in Tourniquet Shock, *ibid.* 60:401-419 (April 13) 1945.

5 per cent of body weight, a value in agreement with that originally found by Blalock, Harkins and others<sup>1</sup> (chart 1).

Along with the local accumulation of fluid, sodium enters the injured area; this amounts to 0.10 milliequivalent for a 15 Gm. mouse and is greater by 0.03 milliequivalent than the amount which can be accounted for by the local increase in fluid. This local increase in sodium is equivalent to the entire sodium in the circulating blood or one fourth of that in the total extracellular fluid. This rapid accumulation of fluid and sodium occurs at the expense of the uninjured tissues, which are correspondingly dehydrated.

During the same two hour period, the injured area loses approximately one third of its total potassium, amounting to 0.03 milliequivalent per 15 Gm. mouse (chart 1). This quantity of potassium is thus released from the traumatized area into the rest of the body; its significance will be discussed later. It is of interest that the potassium loss from the injured area corresponds approximately to the sodium gain, which is in excess of that calculated to enter with the edema fluid, suggesting that an exchange of potassium

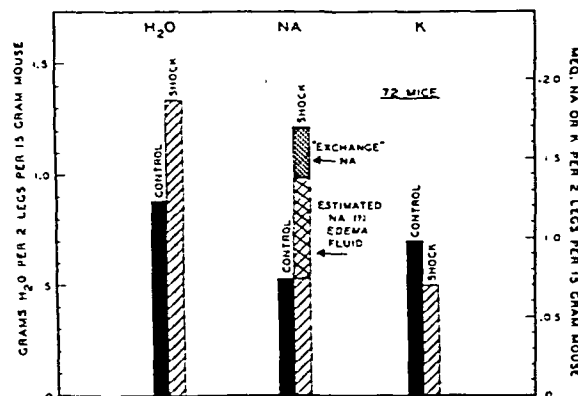


Chart 1.—Changes in water, sodium and potassium in the hindlegs of mice subjected to tourniquets for two hours. Analyses two hours after removal of tourniquets. Values represent the total amounts in the two legs of a 15 Gm. mouse. Control values from normal mice studied simultaneously.

for sodium takes place in injured tissues; evidence that this can occur *in vitro* has been presented by Eichelberger and Hastings<sup>6</sup> and that it can occur *in vivo* by Manery and Solandt.<sup>7</sup>

6. Hastings, A. B., and Eichelberger, L.: The Exchange of Salt and Water Between Muscle and Blood: I. The Effect of an Increase in Total Body Water Produced by the Intravenous Injection of Isotonic Salt Solutions, *J. Biol. Chem.* **117**:73-93 (Jan.) 1937.

7. Manery, J., and Solandt, D.: Studies in Experimental Traumatic Shock with Particular Reference to Plasma Potassium Changes, *Am. J. Physiol.* **138**:499-511 (Feb.) 1943.

The magnitude of these local changes in fluid and electrolyte have also been studied by Fox and Keston<sup>8</sup> with the use of radioactive sodium, and our results are substantially in agreement.

#### URINARY STUDIES

In addition to local alterations in the injured area, some estimate of the electrolyte changes

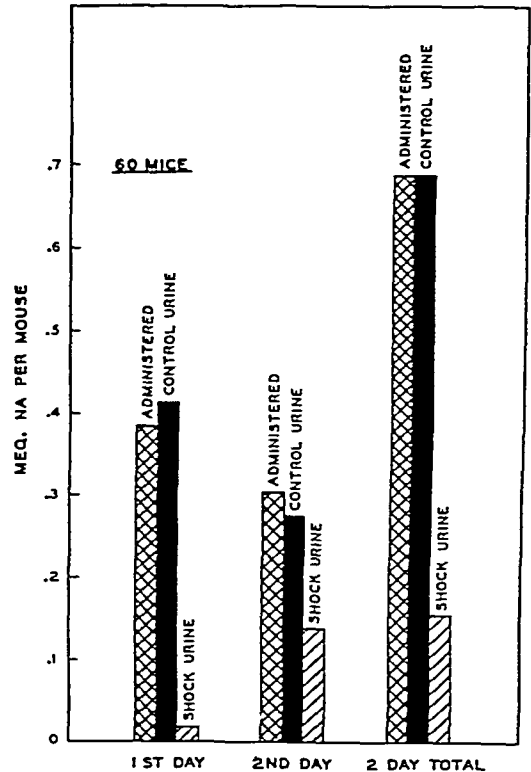


Chart 2.—Sodium excretion in urine of normal and shocked (tourniquet) mice. Both groups received 0.385 milliequivalent of sodium orally the first day and 0.302 milliequivalent the second day. Practically complete retention the first day and 72 per cent retained in forty-eight hours. Nine-tenths per cent solution of sodium chloride was administered.

that are occurring in the rest of the body and of fluid and electrolyte needs in shock may be obtained by urinary studies. Mice in which death from shock was prevented by therapy with 0.9 per cent solution of sodium chloride were placed in metabolism cages for quantitative collection of urine. Normal animals similarly treated with sodium chloride served as a basis for comparison.

The quantity of sodium retained by the shocked animal after administration of isotonic solution of sodium chloride may serve as some index of

8. Fox, C. L., Jr., and Keston, A. S.: The Mechanism of Shock from Burns and Trauma Traced with Radiosodium, *Surg., Gynec. & Obst.* **80**:561-567 (June) 1945.

the sodium requirement during the shock period. The local accumulation of fluid in the injured area is only a partial indication of this deficit; this was shown by Fox<sup>9</sup> in burned patients and in shocked mice. We have similarly found in tourniquet-shocked mice that when 0.38 milliequivalent of sodium per mouse is administered on the first day and 0.3 milliequivalent on the second day there is complete retention during the first twenty-four hours and only 28 per cent of the total amount is excreted during the second twenty-four hour period (chart 2). This retention in terms of isotonic solution of sodium chloride is approximately 20 per cent of the body weight of the animal.

## SIGNIFICANCE OF CHANGES

What importance can be attributed to the fluid and electrolyte disturbances, and what is their significance in terms of therapy?

First, they indicate a dehydration of the sodium-containing extracellular fluid compartment.<sup>10</sup> Since the blood constitutes only one fourth of this reservoir and since the sodium and fluid loss is as great as or greater than the total amounts contained in the plasma, the major deficit must occur in the tissues. It is not to be expected that a normal plasma volume can be maintained with any permanency until the tissue dehydration is also corrected. This con-

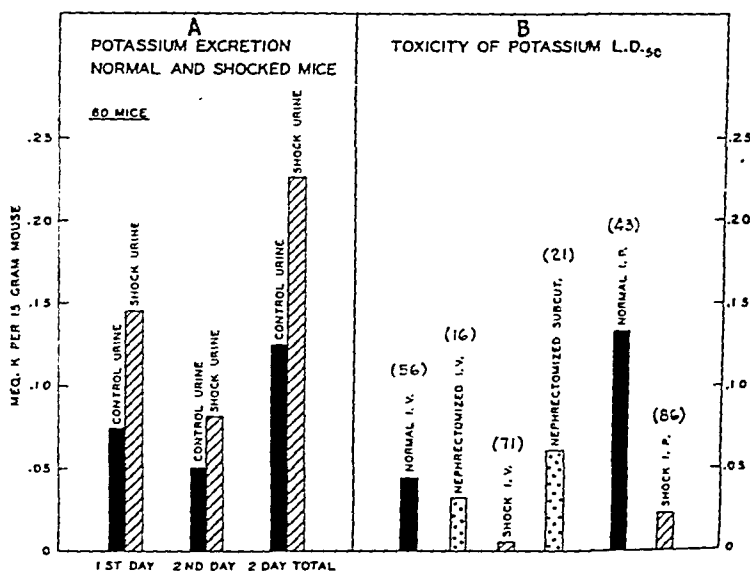


Chart 3.—A, potassium excretion in normal and in shocked mice. Determinations on the same urines used for sodium analyses (chart 2).

B, the L.D.<sub>50</sub> (lethal dose for 50 per cent of animals) of potassium for normal mice intravenously and intraperitoneally, for nephrectomized mice intravenously and subcutaneously and for shocked mice intravenously and intraperitoneally. The toxicity for shocked animals is increased six to nine times over normal. Figures in parentheses indicate number of animals used.

That this retention of sodium is not due to anuria is indicated by the fact that during this period potassium is excreted in excess. Increases above the control values amounting to 0.075 milliequivalent per mouse on the first day and 0.025 milliequivalent on the second day were obtained (chart 3). This has been shown to be more than twice the amount of potassium that is liberated from the injured area in treated mice, indicating that potassium is also released from nontraumatized areas in shock.<sup>5</sup>

9. Fox, C. L., Jr.: Oral Sodium Lactate in the Treatment of Burn Shock, *J. A. M. A.* **124**:207-212 (Jan. 22) 1944. Fox and Keston.<sup>8</sup>

clusion is also corroborated by the therapeutic studies reported later, which reveal that optimum survival from a fatal degree of trauma is not achieved until 10 to 15 per cent of the body weight of isotonic solution of sodium salts is administered.

Second, the quantity of potassium released in the body suggests that a reevaluation be made of its significance as a toxic factor in shock. On

10. (a) Gamble, J. L.: *Chemical Anatomy, Physiology, and Pathology of Extracellular Fluid*, Boston, Harvard Medical School, 1942. (b) Hastings, A. E.: *The Electrolytes of Tissues and Body Fluids*, in Harvey Lectures, 1940-1941, Baltimore, Williams & Wilkins Company, 1941, vol. 36, p. 91. (c) Peters, J. P.: Water Exchange, *Physiol. Rev.* **24**:491-531 (Oct.) 1944.

a basis of various experimental evidence, potassium has been suggested in this role.<sup>11</sup> While some recent evidence supports this view,<sup>12</sup> the importance of potassium has not been generally accepted. This is due in part to the fact that previous studies have been confined to changes in the blood or isolated tissues, and consequently quantitative data on the magnitude of the total changes were not available and also because the observed alterations were interpreted in terms of the normal rather than the shocked animal.

The following observations have been made<sup>5</sup> in an attempt to evaluate the significance of the potassium release in traumatic shock:

(a) In a shocked animal the toxicity of administered potassium increases six to nine times above that for a normal animal (chart 3). This is not the result of a general increase in susceptibility to toxic agents, for under similar conditions the toxicity of magnesium and quinidine (used as drug controls) was less than doubled.

(b) The amount of potassium released in shock, as indicated by analyses of the entire injured area and by urinary studies, is toxic for a normal animal when given intravenously or intraperitoneally and for an anuric (nephrectomized) animal when given subcutaneously and is several times the fatal dose for a shocked animal when given by any route (chart 3).

(c) The elevation of serum potassium in the shocked animal cannot be interpreted in terms of the elevation required to kill a normal animal. Rabbits in shock that are killed by injections of potassium chloride show terminal serum potassium levels (13.20 milliequivalent per liter, with a standard error of 0.22) within the same range as those found in shocked rabbits without treatment with potassium chloride that die from shock several hours later (12.08 milliequivalent with a standard error of 0.35). These values are lower than those obtained for normal rabbits that are killed by injections of potassium chloride (16.58 milliequivalent with a standard error of 0.68). These results suggest that the moderate elevations of serum potassium seen in shock may have greater significance than is usually attrib-

uted to them, particularly in relation to the terminal phases of this condition.

Not only is the shocked animal abnormally sensitive to administered potassium. It is possible to produce withdrawal of fluid and sodium from the body by the intraperitoneal injection of dextrose solutions.<sup>13</sup> By the use of this technic, it has been demonstrated that the shocked animal is also highly susceptible to any additional loss of fluid or sodium.<sup>5</sup>

The evidence indicates that these three factors, fluid loss, sodium loss and potassium toxicity, are interdependent. While in shock the magnitude of each change may not in itself be sufficient to produce death, their combined effects augment one another and may have an important influence on mortality in shock.

There are various types and various degrees of shock, in which a variety of other biochemical changes have been shown to exist<sup>14</sup>; like-

13. Schechter, A. J.: Electrolyte and Volume Changes in Fluids Injected into the Peritoneal Cavity, *Yale J. Biol. & Med.* 4:167-185 (Dec.) 1931. Darrow, D. C., and Yannet, H.: Changes in Distribution of Body Water Accompanying Increase and Decrease in Extracellular Electrolyte, *J. Clin. Investigation* 14:266-275 (March) 1935; Metabolic Studies of Changes in Body Electrolyte and Distribution of Body Water Induced Experimentally by Deficit of Extracellular Electrolyte, *ibid.* 15:419-427 (July) 1936.

14. (a) Russell, J. A.; Long, C. N. H., and Engel, F. L.: Biochemical Studies on Shock: Role of Peripheral Tissues in Metabolism of Protein and Carbohydrate During Hemorrhagic Shock in Rat, *J. Exper. Med.* 79: 1-7 (Jan.) 1944. Engel, F. L.; Harrison, H. C., and Long, C. N. H.: Biochemical Studies on Shock: Role of Liver and Hepatic Circulation in Metabolic Changes During Hemorrhagic Shock in Rat and Cat, *ibid.* 79: 9-22 (Jan.) 1944. Russell, J. A.; Long, C. N. H., and Wilhelm, A. E.: Biochemical Studies on Shock: Oxygen Consumption of Liver and Kidney Tissue from Rats in Hemorrhagic Shock, *ibid.* 79:23-33 (Jan.) 1944. (b) Shen, S. C., and Ham, T. H.: Studies on Destruction of Red Blood Cells, *New England J. Med.* 229:701-713 (Nov. 4) 1943. (c) Govier, W. M.: Studies on Shock Induced by Hemorrhage: III. The Correlation of Plasma Thiamin Content with Resistance to Shock in Dogs, *J. Pharmacol. & Exper. Therap.* 77:40-49 (Jan.) 1943. (d) Aub, J. C.; Brues, A. M.; Dubos, R.; Kety, S. S.; Nathanson, I. T.; Pope, A., and Zamecnik, P. D.: Bacteria and the Toxic Factor in Shock, *War Med.* 5:71-73 (Feb.) 1944. (e) Prinzmetal, M.; Freed, S. C., and Kruger, H. E.: Pathogenesis and Treatment of Shock Resulting from Crushing of Muscle, *ibid.* 5: 74-79 (Feb.) 1944. (f) Glenn, W. L.; Muus, J., and Drinker, C. K.: Observations on the Physiology and Biochemistry of Quantitative Burns, *J. Clin. Investigation* 22:451-459 (May) 1943. Perlmann, G. E.; Glenn, W. W., and Kaufman, D.: Changes in Electrolytic Pattern in Lymph and Serum in Experimental Burns, *ibid.* 22:627-633 (July) 1943. (g) Ricca, R. A.; Fink, K.; Katzin, L. I., and Warren, S. L.: Effect of Environmental Temperature on Experimental Traumatic Shock in Dogs, *J. Clin. Investigation* 24:127-139

11. Scudder, J.: Shock: Blood Studies as a Guide to Therapy, Philadelphia, J. B. Lippincott Company, 1940.

12. Bywaters, E. G. L., and Popjak, G.: Experimental Crushing Injury, *Surg., Gynec. & Obst.* 75:612-627 (Nov.) 1942. Bywaters, E. G. L.: Ischemic Muscle Necrosis, *J. A. M. A.* 124:1103-1109 (April 15) 1944. Clarke, A. P. W., and Cleghorn, R. A.: Chemical Studies of Tissue Changes in Adrenal Insufficiency and Traumatic Shock, *Endocrinology* 31:597-606 (Dec.) 1942.

wise, unknown factors remain to be discovered. The aforementioned concept does not preclude the possibility that such factors may also play a primary or secondary role in death from shock.

#### THERAPEUTIC STUDIES

It should be made clear that the observations on therapy are concerned with the first forty-eight hours following experimental trauma. While delayed deaths rarely occurred after tourniquet shock or hemorrhage, following burns a progressive loss of weight with death within three weeks was frequently seen. This condition was observed regardless of the type of early therapy and is not to be confused with the mortality during the shock phase.

It should also be pointed out that we have been unable to produce delayed hemorrhagic shock in mice or rats with sufficient constancy to employ such a technic for evaluation of therapy. The following results are accordingly based on acute death from loss of blood, as outlined at the beginning of this paper.

Even when every effort has been made to obtain uniformity of conditions, variations in therapeutic response may occur from one day to another, particularly if the environmental temperature is not controlled. The dominant influence of temperature on therapeutic response is discussed in the following paragraphs.

It is believed that for accurate evaluation of experimental therapy two conditions must be met: simultaneous comparisons and an adequate number of comparisons. Even under our laboratory conditions, with standardized trauma, with relative uniformity of animals as to size, sex and diet, with constant environmental temperature and with simultaneous comparisons, at least 30 to 40 animals in each group are necessary for results within 20 per cent accuracy. Conclusions based on 15 animals may be subject to an error as high as 50 per cent.

(March) 1945. Ricca, R. A.; Fink, K.; Steadman, L. T., and Warren, S. L.: Distribution of Body Fluids of Dogs in Traumatic Shock, *ibid.* **24**:140-145 (March) 1945. Ricca, R. A.; Fink, K., and Warren, S. L.: Effect of Sulfadiazine, Antitoxins, Globulins and Dog Plasma on Dogs in Traumatic Shock Under Sodium Pentobarbital Anesthesia, *ibid.* **24**:146-148 (March) 1945. Katzin, L. I.; Ricca, R. A., and Warren, S. L.: Effect of Environmental Temperature and Anesthesia on Survival of Tourniquet Shock in Rabbits, *ibid.* **24**:149-151 (March) 1945. Katzin, L. I., and Warren, S. L.: Thiamine-Deficient Diet in Tourniquet Shock in Rats, *ibid.* **24**:152-153 (March) 1945. Scholz, D. E., and others: Study of Body Temperature and Water Content in Shock Produced by Continuous Intravenous Injection of Adrenalin, With and Without Anesthesia, *ibid.* **24**:154-159 (March) 1945. Footnote 12.

If this variability is observed under controlled conditions in the laboratory, it is important to the clinician to realize the fallacy of basing conclusions on mortality data from small groups of cases, in which no approach to uniformity can possibly be attained.

The results which we have obtained in the three types of experimental injury have shown a similarity in response to fluid and electrolyte therapy that indicates an underlying disturbance common to all of them. After a fatal degree of burn, trauma or hemorrhage, the majority of animals will survive if 10 to 15 per cent of their body weight of an isotonic solution of a sodium salt is administered by any route (charts 4 and 5).

With the exception of the earlier observations of Davidson<sup>15</sup> and Underhill<sup>16</sup> and the more recent studies of Allen,<sup>17</sup> these results could not be anticipated from the previous work in this field.<sup>1</sup> However, experiments in agreement with these observations have been recently made by Fox<sup>8</sup> and Prinzmetal<sup>18</sup> on mice, by Katz, Friedberg and Asher,<sup>19</sup> Swingle and Kleinberg,<sup>20</sup> Warren, Merrill and Stead,<sup>21</sup> Scott, Worth and Robbins<sup>22</sup> and Moyer and colleagues<sup>23</sup> on dogs and by Locke<sup>24</sup> and Harkins<sup>25</sup> on rats.

15. Davidson, E. C.: Sodium Chloride Metabolism in Cutaneous Burns and Its Possible Significance for a Rational Therapy, *Arch. Surg.* **13**:262-277 (Aug.) 1926.

16. Underhill, F. P.: The Significance of Anhydremia in Extensive Superficial Burns, *J. A. M. A.* **95**:852-857 (Sept. 20) 1930.

17. Allen, F. M.: Physical and Toxic Factors in Shock, *Arch. Surg.* **38**:155-180 (Jan.) 1939; Theory and Therapy of Shock: Varied Fluid Injections, *Am. J. Surg.* **62**:80-104 (Oct.) 1943.

18. Prinzmetal, M.; Hechter, O.; Margoles, C., and Feigen, G.: A Principle from Liver Effective Against Shock Due to Burns, *J. Clin. Investigation* **33**:795-806 (Sept.) 1944. Hechter, O.; Bergman, H. C., and Prinzmetal, M.: Comparison of Therapeutic Effectiveness of Serum and Sodium Chloride in Scald Shock, *Am. Heart J.* **29**:484-492 (April) 1945.

19. Katz, L. N.; Friedberg, L., and Asher, R.: Efficacy of Isotonic Sodium Chloride and Glucose in Preventing Shock Following Venous Occlusion of a Limb in the Dog, *Am. J. Physiol.* **140**:65-71 (Oct.) 1943.

20. Swingle, W. W., and Kleinberg, W.: Plasma, Gelatin and Saline Therapy in Experimental Wound Shock, *Am. J. Physiol.* **141**:713-721 (July) 1944.

21. Warren, J. V.; Merrill, A. J., and Stead, E. A. Jr.: The Role of the Extracellular Fluid in the Maintenance of a Normal Plasma Volume, *J. Clin. Investigation* **22**:635-641 (Sept.) 1943.

22. Scott, C. C.; Worth, H. W., and Robbins, E. B.: Comparative Value of Some Blood Substitutes Used in Treatment of Experimental Shock, *Arch. Surg.* **49**:315-318 (April) 1944.

23. Moyer, C. A.; Collier, F. A.; Job, V.; Vaurio, H. H., and Marty, D. A.: Study of the Interrelation-

Therapy in most experiments on burns and tourniquet shock was begun one-half to one hour after the injury, when visible symptoms of shock, namely prostration and dyspnea, were present. Deaths in untreated animals had already occurred at the time therapy was begun. Even when therapy was delayed beyond this point, favorable responses to administration of saline solution have been obtained. In hemorrhage experiments 10.5 per cent of the mice had died at the time of onset of therapy, which was administered in the interval between bleedings (after a blood loss of 2.25 per cent body weight).

The percentage of survivors is considerably lower if only 5 per cent of body weight of an isotonic solution of a sodium salt is given (chart 4); this, in part, explains the lack of

ion. A similar response was obtained with all the sodium salts we have tested, while other cations—potassium, calcium, magnesium, cesium, rubidium and lithium—were either deleterious or without effect.<sup>26</sup>

Likewise, isotonic dextrose solutions had little effect (chart 5); given intraperitoneally (and this probably applies to other methods of administration such as hypodermoclysis), they were decidedly harmful<sup>5</sup> because they temporarily withdrew water and sodium from the body. Hypertonic solutions in general were found to be less effective than isotonic solutions, perhaps for the same reason.

Water administered orally, 8 to 10 per cent body weight, was ineffective in burn shock (91 per cent mortality in 50 mice as compared with 95 per cent in 50 controls). In tourniquet

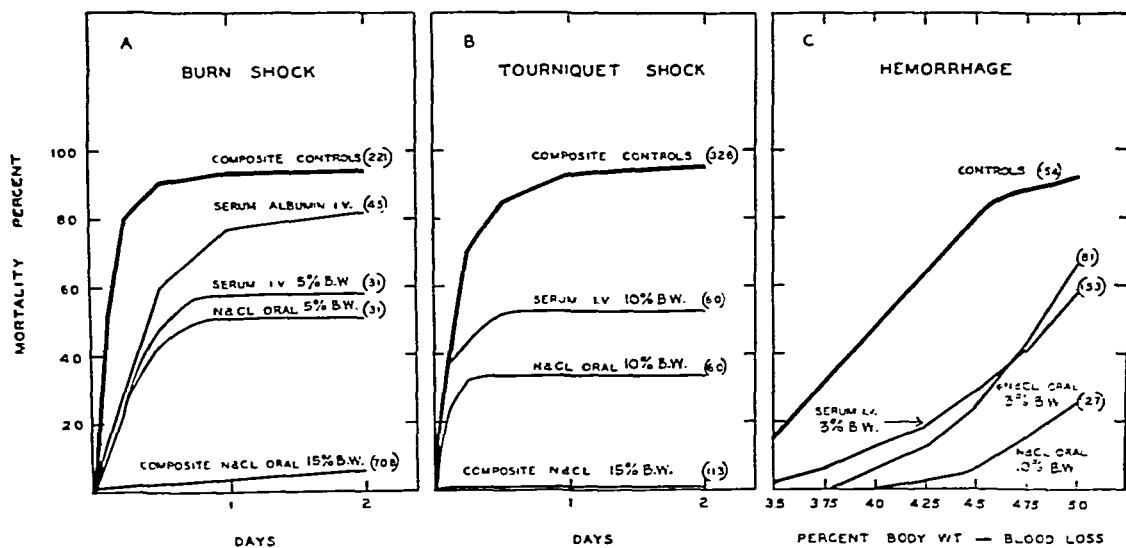


Chart 4.—The similar therapeutic response of mouse serum administered intravenously and saline solution administered orally in burn and tourniquet shock and hemorrhage, given in equivalent doses on a basis of body weight (B.W.). Concentrated human serum albumin (25 per cent) is less effective than serum in doses with equivalent protein content but less sodium chloride. Also the increased effectiveness of larger doses of isotonic solution of sodium chloride (10 to 15 per cent body weight) is indicated. Each curve is a composite of results of several experiments. Figures in parentheses indicate number of mice represented.

success with saline therapy frequently reported from the laboratory and clinic, where this amount has usually represented the maximum therapeutic dose.

A comparison of various salts has shown that the beneficial effect is a function of the sodium

ship of Salt Solutions, Serum and Defibrinated Blood in the Treatment of Severely Scalded, Anesthetized Dogs, *Ann. Surg.* 120:367-376 (Sept.) 1944.

24. Locke, W.: An Experimental Method for Evaluating Blood Substitutes, *Science* 99:475-476 (June 9) 1944.

25. Harkins, H. N.: Personal communication to the authors.

shock some benefit from this was seen (50 per cent mortality in 48 mice as compared with 90 per cent in 48 controls). In hemorrhage only slight benefit from water was obtained,<sup>4</sup> and this was shown to be due to blood dilution: in terms of hemoglobin loss, the animals treated with water were able to withstand no greater depletion than the controls.

Fruit juices, because of their high potassium content, are definitely harmful in experimental shock. An experiment in tourniquet shock demonstrated that 5 per cent body weight of



orange juice by mouth was rapidly lethal (chart 5B).

These results with various electrolytes and fluids, along with the demonstrated sodium deficiency, clearly indicate that in the therapy of shock, fluids other than isotonic solutions of sodium salts may have little value or may even be harmful.

Sodium lactate was employed by Fox<sup>27</sup> in the first clinical appraisal of therapy with oral administration of large amounts of isotonic solutions

#### THERAPY WITH SERUM, PLASMA AND WHOLE BLOOD

It is fundamental to the problem to recognize that in shock there occurs a disturbance of fluid and electrolytes in the blood and tissues, which if corrected as far as possible will result in a high percentage of survivals. The problem presents itself as to what additional therapy will prove of benefit.

There are other known factors, such as protein losses, anoxia, decreased blood volume, ac

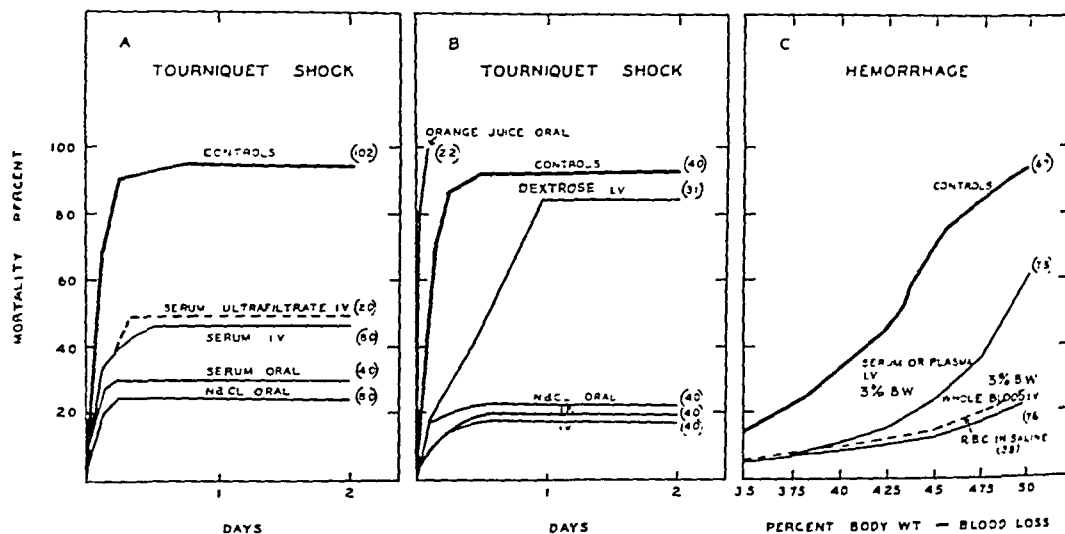


Chart 5.—A, the similar therapeutic response of mouse serum given orally and intravenously, a protein-free ultrafiltrate of serum administered intravenously, and 0.9 per cent solution of sodium chloride given orally in amounts of 8 to 10 per cent body weight. B, equal effectiveness of 0.9 per cent solution of sodium chloride given orally, intraperitoneally and intravenously and the slight effect of 5.5 per cent dextrose administered intravenously in amounts of 10 per cent body weight. The harmful effect of orange juice given orally in 5 per cent of body weight. C, the superiority of whole blood over serum or plasma in hemorrhage; equal effectiveness of whole blood and erythrocytes in saline solution. All curves are composite of results of several experiments, with the number of mice for each curve shown in parentheses.

of sodium salts, and he has reported promising results. Isotonic solutions of this salt (1.75 per cent) are palatable by mouth and withstand boiling for parenteral injection. The lactate ion serves to correct the acidosis that is present in varying degrees in shock. With the amounts required, however, the possibility of producing alkalosis exists. While Fox has found that this hazard is not important when careful observation under hospital conditions can be enforced, for general use a mixture of 1 part of 1.75 per cent solution sodium lactate with 2 parts of 0.9 per cent solution of sodium chloride would seem preferable. This mixture has been recommended by the Shock Committee of the National Research Council.<sup>27</sup>

dosis, infection and undoubtedly unknown ones, which may contribute to the mortality in shock. It is important to know whether such disturbances are primary or secondary and, if possible, to evaluate their influence on mortality by means of experimental therapy.

In burn or traumatic shock and in death from hemorrhage in the mouse, the therapeutic effect of serum or plasma could be accounted for by the amount of isotonic sodium which they contain. We have been unable to demonstrate an effect on mortality attributable to the administration of serum or plasma proteins. A comparison of certain amounts of mouse serum or plasma with equal quantities of isotonic saline solution has shown no significant difference in response in these three forms of trauma (chart 4).

A more exact analysis was attempted by comparing the electrolytes in serum with the original serum. This was accomplished by employing

27. Shock Report 57, Committee on Medical Research, National Research Council, Feb. 9, 1945.

protein-free ultrafiltrate of serum along with the same serum and also by comparison of serum given by mouth (whereby the proteins as such would not be absorbed) with serum administered intravenously. In these experiments<sup>28</sup> likewise, the therapeutic response could be attributed to the electrolytes contained in the serum (chart 5 A). The results with serum albumin (human) were inferior to those with saline solution or serum and here, again, could be correlated with the amount of electrolyte solution (isotonic solution of sodium chloride) contained in the preparation (chart 4 A).

In contrast to the absence of influence of administration of serum protein was the better therapeutic effect observed in hemorrhage when whole blood or erythrocytes in isotonic solution of sodium chloride were compared with plasma or saline solution alone (chart 5 C).

We have carried out similar studies with whole blood therapy for traumatic and burn shock and were unable to demonstrate any superiority over plasma or isotonic solution of sodium chloride similarly administered. In tourniquet shock, treatment with whole blood, 5 per cent body weight intravenously, brought about a survival of 35 per cent of 32 mice while with plasma 40 per cent survived. In burn shock, similar treatment with whole blood resulted in 42 per cent survivals as compared with 66 per cent with plasma. Thirty to 32 mice were employed in each group, and the control mortalities (untreated mice) were 100 per cent in both experiments.<sup>29</sup>

It is thus observed that under these experimental conditions therapy with whole blood is of value in hemorrhage, but in burn or traumatic shock no superiority over plasma or saline solution could be demonstrated. These observations are of particular interest in view of the recent use of whole blood in the treatment of all forms of shock.

#### OTHER FACTORS

Brief mention will be made of some other factors which we have studied in shock. The harmful effect of an environmental temperature that is too hot or too cold is now well recognized<sup>30</sup>; the exact optimum remains to be

established but available evidence indicates that it lies between 16 and 24 C.<sup>30a</sup>

Administration of 100 per cent oxygen at atmospheric pressure did not affect mortality of burn or tourniquet shock in mice<sup>29</sup>; Frank and Fine have previously reported negative results with oxygen at a pressure of 3 atmospheres for dogs.<sup>31</sup> Morphine in analgesic doses (2 to 6 mg. per kilogram) had no unfavorable influence on burn shock in mice<sup>29</sup>; Blalock has previously reported similar results in dogs.<sup>32</sup> Injection of adrenal cortex extract either prophylactically or subsequent to burns did not affect the acute mortality. Likewise, no therapeutic effect was observed from therapeutic doses of epinephrine in oil or from posterior pituitary extracts.<sup>29</sup> In local therapy of burns, covering two thirds or more of the body surface with tannic acid, liquid petrolatum or cod liver oil was deleterious in that the mortality from shock was increased.<sup>2a</sup>

The immunity which has been observed after repeated trauma has been shown to be a local tissue response rather than a humoral reaction.<sup>33</sup>

#### COMMENT

With simplified procedures it has been possible to study the acute mortality following burns, trauma and hemorrhage in large numbers of small animals. The correction of disturbances of fluids and specific electrolytes has been demonstrated to be of greater importance for survival than the administration of plasma proteins. Our results indicate that for the most favorable response quantities of isotonic solutions of sodium salts equal at least to 10 per cent of body weight are indicated during the first twenty-four hours. In this respect, it is believed that current methods of treating shock are inadequate.

by Environmental Temperature, *Proc. Soc. Exper. Biol. & Med.* **51**:350-351 (Dec.) 1942. Rosenthal,<sup>2a</sup> Ricca, Fink, Katzin and Warren.<sup>14f</sup>

30a. More recent studies of temperature effects<sup>29</sup> have shown that the increased survival time of untreated animals kept at 16 to 22 C. is not a true criterion of optimum temperature. When mice with tourniquet shock are treated with adequate amounts of isotonic solution of sodium chloride or plasma, an entirely different response is obtained; the majority of them will live if kept at 26 to 29 C., while the majority of them will die if kept below 22 C. or above 31 C.

31. Frank, H. A., and Fine, J.: Traumatic Shock: V. A Study of the Effect of Oxygen on Hemorrhagic Shock. *J. Clin. Investigation* **22**:305-313 (March) 1943.

32. Blalock, A.: Effects of Morphine in Experimental Shock Due to Hemorrhage. *Arch. Surg.* **47**:326-328 (Oct.) 1943.

33. Rosenthal, S. M.; Tabor, H., and Lillie, R. D.: The Local Nature of Acquired Resistance to Trauma, *Am. J. Physiol.* **143**:402-406 (March) 1945.

28. Rosenthal,<sup>2</sup> Tabor, Kabat and Rosenthal.<sup>4</sup>

29. Unpublished results.

30. Gatch, W. D., and Wakim, K. G.: Effect of External Temperature on Shock: Experimental Study, *J. A. M. A.* **121**:903-907 (March 30) 1943. Cleghorn, R. A.: The Effect of Different Environmental Temperatures on the Survival of Dogs After Severe Bleeding, *Canad. M. A. J.* **49**:363-367 (Nov.) 1943. Elman, R.; Cox, W. M.; Lischer, C., and Mueller, A. J.: Mortality in Severe Experimental Burns as Affected

Of practical importance is the fact that oral therapy is efficacious in the treatment of shock. The administration of these large volumes of isotonic saline solution can be accomplished most easily and with the least hazard if they are given in large part by mouth (or through stomach tube, if necessary). Such treatment can be carried out in the absence of equipment for intravenous injections or trained personnel. However, for a patient in severe collapse or coma, when death may be imminent, when intestinal absorption may be slow or when, for any reason, oral medication is difficult, oral therapy alone should not be relied on and intravenous or other routes of administration should be given preference.

The experimental results would seem to justify clinical trial of oral electrolyte therapy for shock as a first aid or an emergency measure in civilian and military practice, since it can be employed under the simplest conditions and, when the emergency demands, can be adapted to self medication.

It should be emphasized that these observations are concerned only with the first forty-eight hours following injury and also that infec-

tions or other complications which may occur require individual attention.

#### SUMMARY AND CONCLUSIONS

The sodium, potassium and fluid changes have been studied quantitatively in traumatic shock in mice. The magnitude of these alterations and the high susceptibility of shocked animals to experimentally produced increases in these changes suggest that their combined effects may play an important role in the mortality from shock.

A high percentage of animals will survive an otherwise fatal burn, trauma or hemorrhage if isotonic solutions of sodium salts in amounts equivalent to 10 to 15 per cent of body weight are administered by any route during the first twenty-four hours. The effect of the electrolyte is a function of the sodium ion.

It is believed that current methods of treating shock are inadequate in regard to the quantity of isotonic sodium solution employed.

Experimental evidence indicates that this therapy may be of value as a first aid prophylactic measure, as well as in the treatment of shock, in military and civilian practice.

# GELATIN SPONGE. A NEW HEMOSTATIC SUBSTANCE

## STUDIES ON ABSORBABILITY

HILGER PERRY JENKINS, M.D., AND JAMES S. CLARKE, M.D.

CHICAGO

Hemostasis is a fundamental principle in surgical technic. It can be satisfactorily obtained in most instances by ligature, clips, pressure, electrocoagulation and packs. There are some situations, however, in which venous or capillary bleeding may be difficult to control by these methods. This is especially true of neurosurgical operations in which bleeding from the dura, the brain or the spinal meninges may be especially troublesome. This also obtains in many instances of general surgical procedures, such as operations on liver, kidney, spleen, pancreas, thyroid, bone, chest and female generative tract, in which conventional hemostatic methods may not be adequate. Ways and means of obtaining better hemostasis in such circumstances would constitute a substantial improvement in the general technic of surgery.

The major recent advances in the problem of control of capillary and venous oozing have been the development of coagulating agents, such as thrombin, and the use of absorbable substances which will aid in clot formation by purely mechanical means, such as transmitting pressure to the bleeding surface and offering a matrix for the formation of the clot. The clot-forming properties of these substances are presumed to be enhanced by the addition of the thrombin. The use of muscle stamps, which was introduced by Cushing<sup>1</sup> in 1911 and has been rather widely used in neurosurgical procedures since that time, constitutes the first general use of these principles, in that the muscle transmits some pressure, is absorbed and contains a clot-promoting substance.<sup>2</sup>

From the Department of Surgery, University of Chicago, The School of Medicine.

This work was aided in part by a grant from The Upjohn Company, Kalamazoo, Mich.

1. Cushing, H.: *The Control of Bleeding in Operations for Brain Tumors, with the Description of Silver Clips for the Occlusion of Vessels Inaccessible to the Ligature*, Ann. Surg. 54:1, 1911.

2. Fonio, A.: *Ueber die Wirkung der intravenösen und der subkutanen Injektion von Koagulen Kocher-Fonio am Tierversuch, nebst einigen therapeutischen Erfahrungen*, Mitt. a. d. Grenzgeb. d. Med. u. Chir. 27:642, 1914.

The work of Seegers<sup>3</sup> and his co-workers deserves special mention as a major contribution to the problem of hemostasis. They have developed a method of preparing a purified thrombin, which is now commercially available, and, furthermore, they have worked out a method of calibration and standardization of the potency of the thrombin known as the Iowa unit. There have been commercial preparations of thrombin or clot-promoting substances obtained from muscle or tissue extracts which have been available on the market for many years. This type of material has been outmoded, however, since the work of the Iowa group.

From the standpoint of absorbable substances which could mechanically aid in the formation of a clot, the work of Frantz<sup>4</sup> deserves attention. She found that oxidized cellulose in the form of absorbable cotton, paper or gauze was absorbed in eleven to thirty days in dogs and cats and produced only a mild foreign body reaction. She and co-workers reported the successful use of oxidized cellulose without thrombin to control bleeding in 17 cases in which muscle would otherwise have been required for hemostasis. Putnam<sup>5</sup> used oxidized cellulose soaked in thrombin to control bleeding in thirty neurosurgical operations and found it satisfactory. Cronkite, Deaver and Lozner<sup>6</sup> have been favorably impressed with the use of thrombin with and without oxidized cellulose to arrest hemorrhage in operative and traumatic wounds. The observations of Uihlein

3. Seegers, W. H.; Warner, E. D.; Brinkhouse, K. M., and Smith, H. P.: *The Use of Purified Thrombin as a Hemostatic Agent*, Science 89:86, 1939. Seegers, W. H., and Doub, L.: *Oxidized Cellulose and Thrombin*, Proc. Soc. Exper. Biol. & Med. 56:72, 1944.

4. Frantz, V. K.: *Absorbable Cotton, Paper and Gauze*, Ann. Surg. 118:116, 1943. Frantz, V. K.; Clarke, H. T., and Lattes, R.: *Hemostasis with Absorbable Gauze*, *ibid.* 120:181, 1944.

5. Putnam, T. J.: *The Use of Thrombin on Soluble Cellulose in Neurosurgery*, Ann. Surg. 118:127, 1943.

6. Cronkite, E. P.; Deaver, J. M., and Lozner, E. L.: *Experiences with Use of Thrombin With and Without Soluble Cellulose for Local Hemostasis*, War Med. 5:80 (Feb.) 1944.

and colleagues<sup>7</sup> on the use of oxidized cellulose and thrombin has been favorable in 57 out of 60 cases at the Mayo Clinic.

One of the most significant contributions to hemostasis has resulted from the large scale plasma fractionation program conducted by the department of physical chemistry of the Harvard Medical School. One of the products of this fractionation of human plasma was fibrin foam,

the cerebral cortex of monkeys. It was found that the foam soaked in thrombin had a hemostatic action, was absorbed and caused a minimum tissue reaction. They reported on its use in operations on 34 patients and felt that it had a number of advantages over muscle as a hemostatic agent. Woodhall<sup>10</sup> reported on the use of fibrin foam soaked in thrombin in 226 neurosurgical operations and found that a desirable



Fig. 1.—Gelatin sponge in liver after two days. The architecture of the sponge is well demonstrated. The interstices are partially filled with red blood cells, and at the junction with the liver there are a few polymorphonuclear leukocytes. There is no evidence of tissue reaction in the liver parenchyma.

which Bering<sup>8</sup> described in 1944. This material was tested by Ingraham and Bailey<sup>9</sup> in and on

7. Uihlein, A.; Clagett, O. T.; Osterberg, A. E., and Bennett, W. A.: Absorbable Oxidized Cellulose with Thrombin as a Hemostatic Agent in Surgical Procedures, *Surg., Gynec. & Obst.* 80:470, 1945.

8. Bering, E. A.: Chemical, Clinical, and Immunological Studies on the Products of Human Plasma Fractionation: XX. The Development of Fibrin Foam as a Hemostatic Agent and for Use in Conjunction with Human Thrombin, *J. Clin. Investigation* 23:586, 1944.

9. Ingraham, F. D., and Bailey, O. T.: The Use of Products Prepared from Human Fibrinogen and Human Thrombin in Neurosurgery. Fibrin Foams as Hemostatic Agents, Fibrin Films in Repair of Dural Defects and in Prevention of Meningocerebral Adhesions, *J. Neurosurg.* 1:23, 1944. Ingraham, F. D.; Bailey, O. T., and Nulsen, F. E.: Studies on Fibrin Foam as a Hemostatic Agent in Neurosurgery, with

hemostatic effect was obtained. Fibrin foam has been available only in limited quantities and has been restricted in its use to a relatively small group, composed mostly of neurosurgeons.

Special Reference to Its Comparison with Muscle, *ibid.* 1:171, 1944. Ingraham, F. D., and Bailey, O. T.: Clinical Use of Products of Human Plasma Fractionation: III. The Use of Products of Fibrinogen and Thrombin in Surgery, *J. A. M. A.* 126:620 (Nov. 11) 1944. Bailey, O. T., and Ingraham, F. D.: Chemical, Clinical, and Immunological Studies on the Products of Human Plasma Fractionation: XXI. The Use of Fibrin Foam as a Hemostatic Agent in Neurosurgery. Clinical and Pathological Studies, *J. Clin. Investigation* 23:591, 1944.

10. Woodhall, B.: Fibrin Foam as a Hemostatic Agent in Rehabilitation Neurosurgery, *J. A. M. A.* 126:469 (Oct. 21) 1944.

The most recent of the absorbable hemostatic materials is gelatin sponge or foam.<sup>11</sup> This is prepared from ordinary commercial gelatin, which is made up in a solution, to which a hardening agent is added. After bubbles of air are introduced, the mixture is allowed to dry in pans. It can then be cut into any desired size or shape. The material which has been used for experimental purposes has been provided in sealed glass jars previously subjected to sterilization with dry heat. The gelatin sponge is a white crisp material which is extremely light in weight. One cubic centimeter weighs 9 mg. The sponge will take up many times its weight of water when it is submerged and the air bubbles expressed.

additional factor in this evaluation, the gelatin sponge was used without thrombin.

A series of 12 dogs was operated on by ordinary aseptic surgical technic with ether anesthesia. After the abdomen had been opened, incisions were made 2 cm. long and 1 cm. deep in the liver, the kidneys and the spleen. The brisk hemorrhage which resulted from these incisions was controlled by packing the moistened gelatin sponge into the incision and holding it in place for about two minutes with ordinary moistened gauze. When the gauze was removed, the gelatin sponge was usually adherent in the incision and the bleeding stopped. Sometimes there was oozing from the ends of the incision, which was arrested by laying another piece of gelatin sponge over the length of the incision and covering the previously applied sponge. Gelatin sponge was also implanted in the

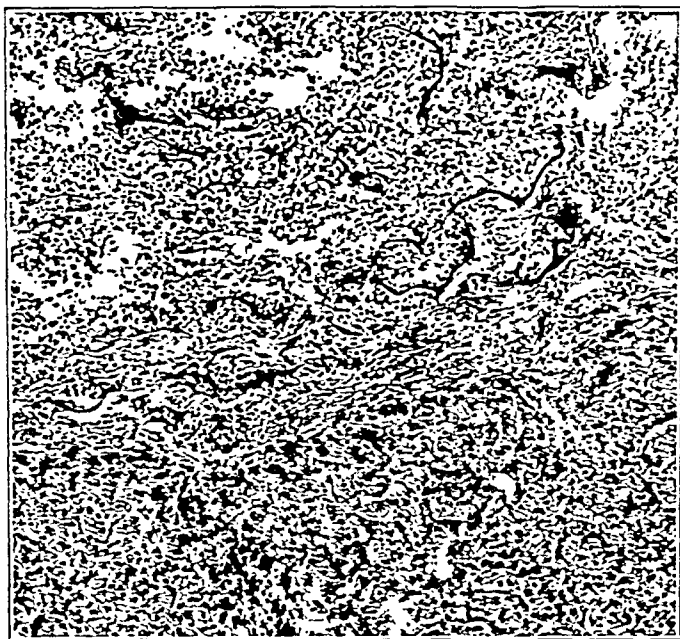


Fig. 2.—Gelatin sponge in liver after seven days. There is a wide zone of polymorphonuclear leukocytic invasion of the sponge at its junction with the liver, the parenchyma of which does not appear to exhibit any inflammatory reaction. The sponge appears to have undergone a considerable degree of absorption, as only fragments remain near the liver.

When moistened, the gelatin sponge shrinks and becomes soft and pliable. It easily adjusts itself to any irregularities in the surface to which it is applied. It does not fragment easily, although it is not especially tough.

#### EXPERIMENTAL STUDY

An experiment was devised primarily to determine the behavior of the gelatin sponge in the tissues of animals and the response of the tissues to the gelatin. To avoid the introduction of an

omentum and in the rectus muscle near the abdominal incision. The animals were killed at periods varying from two to fifty-six days after the implantation. Two of the animals died at two and three days respectively.

At autopsy the sponge could usually be easily identified in the short term implants as a red soggy mass. In the omentum there was an area of induration, in the center of which the sponge could be found if the omentum was cut across at this point. In the abdominal wall one could usually detect a small area of induration along the peritoneal surface (the sponge was put between the posterior sheath and the rectus muscle) which when cut revealed the sponge. After a week or ten days it was often difficult to

11. Correll, J. T., and Wise, E. C.: Certain Properties of a New Physiologically Absorbable Sponge, *Proc. Soc. Exper. Biol. & Med.* 58:233, 1945.

identify the sponge in the abdominal wall, and in the omentum one could find only a slightly indurated area in which the sponge could be found. After two weeks it was difficult to identify the sponge grossly in the omentum. The sponge could usually be easily identified in the early specimens of liver, kidneys and spleen. Varying amounts of fibrinous adhesions were present about the implants in the liver, although such adhesions were not common in the kidneys or the spleen. Implants observed later showed evidence of fibrous adhesions of

which the sponge had been implanted a month or more. In a few instances of short term implants in the liver, there was some evidence of exudate between the sponge and the surface of the liver.

Microscopic sections were made of all the implants which could be identified either grossly or as a residual fibrous adhesion. The gelatin sponge appeared as a meshwork of homogenous hematoxylin-staining material. Where the sponge had been used for hemostasis, as in the liver, the kidneys and the spleen, the interstices of the

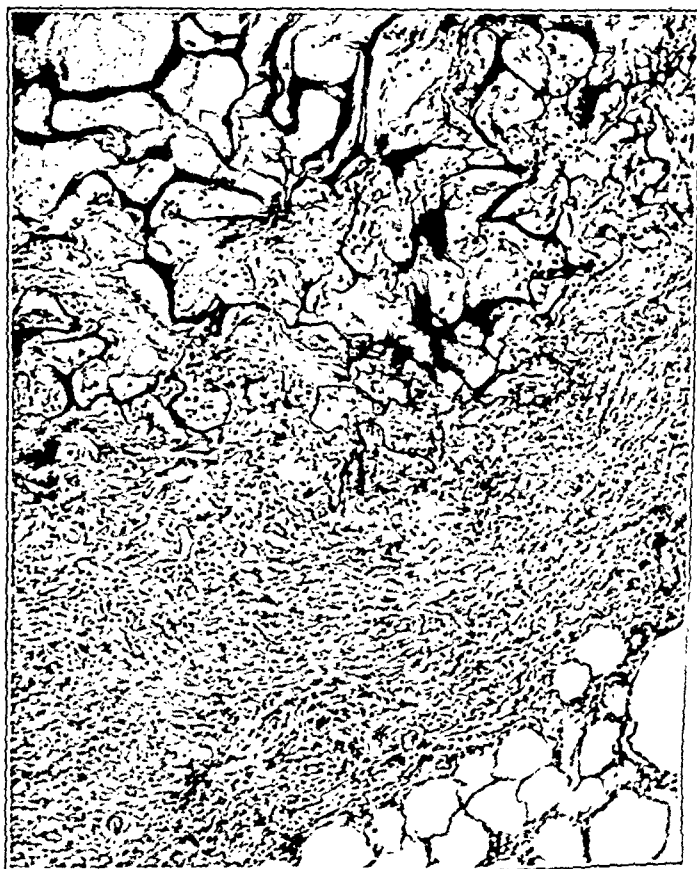


Fig. 3.—Gelatin sponge in omentum after seven days. There is a gradual transition from the central portion of the sponge, where there are only a few invading cells, to the periphery, where there is invasion of the interstices by fibroblasts, polymorphonuclear leukocytes, lymphocytes and macrophages. There is a gradual disintegration of the sponge architecture at the peripheral part, which merges with a surrounding zone of cellular response similar to that seen within the interstices.

varying amount which completely covered any portion of the gelatin sponge. The sponge could be identified in these later specimens only by cutting through the thin layer of fibrous encapsulation, and even then one could not be sure of the presence of any residual gelatin sponge until the microscopic sections were inspected. This was especially true of the specimens in

sponge were seen to be filled for the most part by red blood cells (fig. 1). In some sections there was evidence of invasion of the peripheral portion of the sponge by polymorphonuclear leukocytes. In the instances in which the polymorphonuclear invasion was especially noticeable, there was evidence of absorption of the gelatin sponge (fig. 2 and 3). In most sections

however, there was only a slight invasion of the sponge by polymorphonuclear leukocytes. In addition, there were also lymphocytes and some plasma cells in the peripheral portions.

After a week or more, the predominant cells invading the gelatin sponge were macrophages. There was little tendency for the formation of foreign body giant cells, such as one sees frequently in microscopic sections of suture material such as cotton, silk, linen or chromic surgical

tion became fibrous. In the longer term implants, the fibrous tissue appeared to invade the periphery of the sponge where absorption had occurred as a result of the activity of the macrophages.

In some of the sections there was evidence of the surgical gut suture material which had been used to hold the implant in place. The tissue response to the gut was invariably more pronounced than that observed for the gelatin sponge.



Fig. 4.—Gelatin sponge in liver after twenty-three days. The gelatin sponge is separated from the normal-appearing liver cells by a thin zone of fibrous tissue which merges with and invades the peripheral portion of the sponge. The interstices of the sponge are filled with red blood cells in some areas, and there are a moderate number of macrophages throughout. Polymorphonuclear leukocytes are scarce. There is some thinning out of the walls of the cavernous spaces and some collapsing of the walls, indicative of a moderate degree of absorption.

gut. These macrophages did not form a dense mass of cells, such as one sees at the site of absorption of chromic surgical gut, but rather a more evenly dispersed grouping of cells throughout the interstices of the sponge (figs. 4, 5 and 6).

Fibroblast response was usually observed within a week, producing a definite encapsulation of the sponge. Subsequently this encapsula-

The absorption of the gelatin sponge was apparently most rapid in the presence of polymorphonuclear leukocytes, which appeared to produce a liquefaction of the gelatin sponge. In some such instances, the absorption had progressed almost to completion within twelve days. On the other hand, most of the implants showed evidence of a slower absorption, which appeared to be carried out by macrophages and which



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however, there was only a slight invasion of the sponge by polymorphonuclear leukocytes. In addition, there were also lymphocytes and some plasma cells in the peripheral portions.

After a week or more, the predominant cells invading the gelatin sponge were macrophages. There was little tendency for the formation of foreign body giant cells, such as one sees frequently in microscopic sections of suture material such as cotton, silk, linen or chronic surgical

tion became fibrous. In the longer term implants, the fibrous tissue appeared to invade the periphery of the sponge where absorption had occurred as a result of the activity of the macrophages.

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apparently required as long as five weeks or more to complete the absorption. It is probable that larger pieces of gelatin sponge may require a longer period than this to undergo complete absorption.

#### COMMENT

These experiments have demonstrated that gelatin sponge is a bland substance which is generally slowly absorbed in the tissues over a period of about five weeks. There is apparently some degree of encapsulation and replacement of the gelatin sponge with fibrous tissue during the process of absorption. In the presence of conspicuous numbers of polymorphonuclear leukocytes, the gelatin sponge is rapidly absorbed. This is a point which resembles to some extent the behavior of surgical gut in the tissues. In an extensive study of the absorption of surgical gut,<sup>12</sup> it was found that when gut was rapidly absorbed there was a conspicuous polymorphonuclear leukocytic response, which was apparently responsible for the absorption by a liquefaction process. On the other hand, gut which was relatively slowly absorbed was characterized by a slight initial leukocytic response and a subsequent fibroblast and macrophage response which encapsulated the gut and gradually disposed of it by the phagocytic action of macrophages. In the work on surgical gut, it was found that the instances of conspicuous initial leukocytic response were apparently induced to a greater extent by chemical irritants in the tubing fluid<sup>13</sup> than by irritant properties inherent in the surgical gut. The occasional instances in these experiments on gelatin sponge in which there was a conspicuous leukocytic response were probably due to an inflammatory reaction from bacterial contamination of the wound. The usual observation of a negligible

leukocytic response of the tissues to the gelatin sponge indicates that this is a bland substance which does not possess inherent irritant properties.

It was interesting to observe the mechanical hemostatic action of the gelatin sponge when it was inserted into bleeding incisions in the liver, kidney or spleen. It is probable that this hemostatic action is due to the enormous surface contacts between the blood and the myriads of cavernous spaces in the sponge which take up the blood from the oozing surface. In addition, there is the advantage of the transmission of pressure to the bleeding surface by a substance which does not have to be removed, thus avoiding the recurrence of bleeding so often experienced when one attempts to control the bleeding from an oozing surface by simple pressure of an ordinary piece of gauze, which must be ultimately removed.

Since there is little doubt about the effect of thrombin in promoting clot formation, wherever one wishes to obtain the maximum hemostatic effect one should probably combine the thrombin with the mechanical hemostatic agent. The extent to which the thrombin enhances the hemostatic action of the mechanical hemostatic agents has not as yet been clearly demonstrated. Experiments have been planned which may clarify this point.

The clinical use of this gelatin sponge or foam to aid in the control of bleeding with or without the thrombin has an enormous number of possibilities. It would appear to be useful wherever fibrin foam or oxidized cellulose has been proved to be of value. It is not within the scope of this communication to evaluate the relative merits and limitations of these relatively new hemostatic substances; however, there is a place for some review of the situation from the observations thus far made.

Muscle is not a satisfactory hemostatic agent. It is not freely available without resort to an additional incision. Muscle is not so easily molded to irregular surfaces, and it causes appreciable tissue reaction. According to Ingraham and Bailey, oxidized cellulose is inferior to fibrin foam because its looser structure is less well adapted for hemostasis, it does not adhere to tissues as well and it cuts and molds less easily. Moreover, Seegers and Doub have shown that the carboxyl groups of oxidized cellulose rapidly inactivate thrombin solution unless neutralized with sodium bicarbonate beforehand. Although fibrin foam appears to have an advantage over oxidized cellulose, it is dependent for its production on a large scale program of collection and

12. Jenkins, H. P., and Hrdina, L. S.: Absorption of Surgical Gut (Catgut): I. The Decline in Tensile Strength in the Tissues, *Arch. Surg.* **44**:881 (May) 1942; II. Pepsin Digestion Tests for the Evaluation of Duration of Tensile Strength in the Tissues, *ibid.* **44**:984 (June) 1942. Jenkins, H. P.; Hrdina, L. S.; Owens, F. M., and Swisher, F. M.: Absorption of Surgical Gut (Catgut): III. Duration in the Tissues After Loss of Tensile Strength, *ibid.* **45**:74 (July) 1942. Jenkins, H. P.: Absorption of Surgical Gut (Catgut): IV. Recommendations for Absorbability and Digestibility Specifications, *ibid.* **45**:323 (Aug.) 1942. Dunham, C. L., and Jenkins, H. P.: Surgical Gut Tubing Fluid as a Tissue Irritant, *Ann. Surg.* **118**:269, 1943. Jenkins, H. P., and Dunham, C. L.: Irritant Properties of Tubing Fluids as a Factor in the Tissue Reactions Observed with Surgical Gut (Catgut), *ibid.* **118**:288, 1943.

13. Sinclair, J. A., and Douglas, B.: Local Implantation of Gelatin in Wounds, *Arch. Surg.* **49**:47 (July) 1944.

fractionation of human plasma. It is doubtful whether this source could ever fill the needs of surgeons except as a special material to be used sparingly by a few.

It is hoped that the gelatin sponge or foam may serve the same useful purposes as fibrin foam, as it can be produced in unlimited amounts from materials which are plentiful and cheap. This would make available to the entire membership of the surgical profession a new substance which can be of aid in controlling bleeding when other methods are not applicable.

sponge is apparently rapidly absorbed in the presence of an acute inflammatory reaction in which there is a dense polymorphonuclear leukocytic reaction. Foreign bodies of any type generally cause trouble in the presence of an acute inflammatory process, and it is of interest to know that gelatin sponge will undergo rapid "liquidation" in such circumstances. Thus may be avoided the development of a draining sinus down to the foreign material, which often occurs when the foreign substance is resistant to the action of leukocytes. On the other hand, if



Fig. 5.—Gelatin sponge in kidney after twenty-three days. The gelatin sponge has a thin zone of fibrous tissue at the peripheral portion, which invades the interstices. This zone of fibrous tissue separates the sponge from the kidney parenchyma, which was incised at this point and appears to have healed in, extruding the sponge from the incision. There are red cells in some interstices. Some macrophages have invaded the sponge, which is undergoing a moderate degree of absorption. Cellular response in the section is less than that about most foreign bodies such as surgical gut, linen or silk.

Sinclair and Douglas<sup>13</sup> found that the local implantation of gelatin into wounds leads to an accelerated fibroplasia and increased strength. In the light of these findings, it may be that the gelatin sponge supplies a substance locally which is beneficial to healing of the wound. Another point which should be brought out is that gelatin

there is no excessive leukocytic response to the sponge, it becomes incorporated in the tissues and gradually absorbed by a relatively mild phagocytic cell response.

The gelatin sponge has been used in 15 clinical cases in various ways to determine its behavior in human tissues. It has been used in

incisions in the liver to obtain specimens for biopsy, on the under surface of the liver after cholecystectomy, on thyroid beds after thyroidec-tomy, on dermatome donor areas, in laparotomy wounds and on the surface of granulating wounds. Our observations are too limited to permit us to draw any conclusions other than that bleeding was controlled and there were no complications which might be attributed to the use of the gelatin sponge. When the gelatin is used on granulating wounds, it undergoes ab-

sorption within a day or two. On dermatome donor areas, it usually undergoes absorption in a few days. The clinical and experimental observations thus far made lead us to believe that gelatin sponge could be considered for use in many situations other than neurosurgical operations. It would have a place in resections of bone in which there is troublesome bleeding from

the bone. It certainly would be infinitely better tolerated by the tissues than bone wax. For resections of the liver, it would appear that this might offer a good supplement to suture and electrocoagulation technic. After cholecystec-tomy, one frequently encounters enough bleed-ing from the under surface of the liver that one hesitates to close the abdomen until the bleeding appears to be controlled. Suture of the under surface of the liver is a tedious procedure in some instances, especially when the relaxation of the

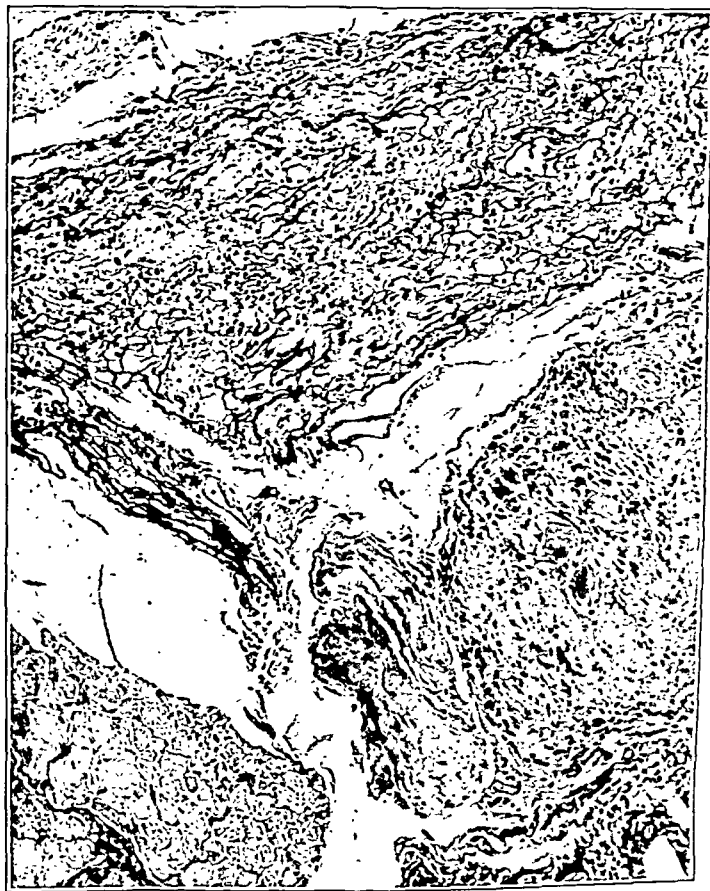


Fig. 6.—Gelatin sponge in abdominal muscles after twenty-three days. The gelatin sponge has collapsed in some places and obliterated the interstices to some extent. The walls of the sponge structure are thin, and the interstices are invaded by fibroblasts, macrophages and lymphocytes in moderate numbers. The gelatin sponge appears to be in a moderately advanced stage of absorption. There is one area where a foreign body giant cell is noticed, which may be due to suture material rather than to sponge, as the gelatin does not appear to stimulate the formation of these foreign body type of giant cells.

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abdomen is not good. Furthermore, one may sometimes create more bleeding by suturing over the raw liver surface than one had originally. This would be an especially suitable place for a hemostatic substance such as gelatin sponge. In gynecologic procedures, one may encounter oo-zing surfaces in the pelvis which are difficult to control by ligatures but which might respond to

this hemostatic substance. Bleeding from tooth sockets can be controlled by gelatin sponge.

The most hopeful use for the gelatin sponge might be as a first aid measure in military combat to pack into bleeding wounds when facilities are not available for the immediate treatment of the wounds. The use of a penicillin solution to moisten the sponge may have sufficient merit that it will be possible to control bleeding as well as infection until the patient is evacuated to a point where facilities permit more adequate care.

There is one point about gelatin sponge which must be considered, the fact that gelatin per se is an extremely good culture medium for bacteria and the introduction into contaminated wounds of a substance which would aid the growth of bacteria would not be without its limitations. It must be considered also that it is desirable to avoid or minimize the use of foreign material in a wound if possible. However, if one has the possibility of a troublesome hematoma to consider, there is justification for utilizing a substance which appears to present fewer hazards to the healing of the wound than a large hematoma.

#### SUMMARY

1. Gelatin sponge or foam was found to be a relatively bland substance which usually undergoes absorption by the phagocytic action of macrophages over a period of about five weeks.

2. The presence of a conspicuous number of polymorphonuclear leukocytes would generally lead to rapid absorption of the sponge within a few days to a week, by a liquefaction process.

3. The magnitude of the tissue reaction to the gelatin sponge during the period of absorption was generally less than that observed for surgical gut.

4. Gelatin sponge has a definite hemostatic action per se when applied to bleeding surfaces with moderate pressure.

#### CONCLUSIONS

Gelatin sponge or foam appears to have properties which make it suitable as an absorbable hemostatic substance and deserves clinical trial in the varied fields of surgery to further evaluate its merits and limitations.

# BREAST CANCER AND "PAGET'S DISEASE OF THE BREAST"

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This study, which has been prompted by the evidence of confusion and the divergence of opinion among clinicians and pathologists alike as to the nature of so-called "Paget's disease of the breast," embraces a thorough review of 29 cases<sup>1</sup> as well as a review of studies and observations by other investigators of this malady. The origin of this dissension emanates from confusion in regard to the cause and the significance of (and, consequently, the therapy indicated for) "Paget's disease." Here an attempt is made to answer the following questions: 1. What is "Paget's disease of the breast"? 2. Is there any cogent evidence as to its etiologic derivation? 3. How should it be treated? 4. Does the name "Paget's disease," which this malady has come to bear, actually clarify or confuse the picture, and is it, therefore, a justifiable eponym?

## HISTORY

In 1874, Sir James Paget recorded in *St. Bartholomew's Hospital Reports*: "I believe it has not yet been published that certain chronic affections of the skin of the nipple and areola are very often succeeded by the formation of scirrhus cancer in the mammary gland. I have seen about fifteen cases in which this has happened, and the events were in all of them so similar that one description may suffice."<sup>2</sup> In this report Paget for the first time called attention to the malady which has since come to bear his name. He described a nipple and areolar eruption which was, he thought, not different from long persistent eczema, psoriasis or other chronic diseases of the skin. "But it has happened that in every case which I have been able to watch, cancer of the mammary gland has followed within at the most two years, and usually within one year."

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1. From Barnard Free Skin and Cancer Hospital, Barnes Hospital and the St. Louis Jewish Hospital.

2. Paget, J.: On Disease of the Mammary Areola Preceding Cancer of the Mammary Gland, *St. Barth. Hosp. Rep.* 10:87-89, 1874.

Paget's description was based on clinical observations only, and it was not until two years later (1876) that microscopic study of the lesion was made by Henry Butlin.<sup>3</sup> He found changes in the galactophorous ducts but no actual cancer. The changes in the dermis he interpreted as eczema and concluded that the changes in the ducts were significant, inasmuch as, even though no cancer was discovered in the 2 patients that he described, it appeared highly suggestive that such might eventually have developed on the underlying duct and gland system. Butlin is generally and mistakenly credited with having been the first to describe the so-called "Paget cells," whereas, in reality, he does not mention these structures. It was in reality Darier, in 1889,<sup>4</sup> who for the first time recorded the description of the "Paget cell," the presence of which in the epidermis is characteristic of this disease. Darier proposed the view that the changes are the result of infestation by a "psorosperm" and that an epithelioma might ensue. The parasitic origin of the disease has since been abandoned as an etiologic factor. Thin, in 1881,<sup>5</sup> was the first to advocate that the lesion of the nipple may be secondary to a carcinoma of the underlying mammary gland.

In 1894 Unna<sup>6</sup> studied the peculiar intraepidermal cells and concluded that they were epidermal cells which had undergone a peculiar type of degeneration. In 1907 Winiwarter<sup>7</sup> claimed to have traced all stages in development from a prickle cell to a characteristic "Paget cell." In 1904 Handley<sup>8</sup> contended that the

3. Butlin, H. T.: On the Minute Anatomy of Two Cases of Carcinoma of the Breast, *Med.-Chir. Tr.* 60: 153-160, 1877.

4. Darier, M. J.: Sur une nouvelle forme de psorosperme cutanee: La maladie de Paget du mamelon. *Compt. rend. Soc. de biol.* 1:294-297, 1889.

5. Thin, G.: On the Connection Between Disease of the Nipple and Areola and Tumours of the Breast. *Tr. Path. Soc. London* 32:218-227, 1881.

6. Unna, P. G.: Die Histopathologie der Hautkrankheiten. Berlin, A. Hirschwald, 1894.

7. von Winiwarter, H.: Ueber Pagetsche Krankheit. *Arch. f. Dermat. u. Syph.* 85:239-262, 1907.

8. Handley, W. S.: Paget's Disease of the Nipple. *Lancet* 1:519-523 (April 7) 1917.

epidermal changes were "nutritional and non-malignant," resulting from filling of the corium and subcutaneous tissue lymphatics with cancer cells originating in the deeper ducts or acini.

In 1900 Darier<sup>4</sup> considered the characteristic Paget changes as due to "dyskeratosis." This view has since found a considerable following. According to Darier, dyskeratosis consists in developmental segregation in the epidermis of a number of malpighian cells, which subsequently develop in an abnormal manner, independent of their fellows. In this group of dyskeratoses he included Bowen's disease, dyskeratosis follicularis, Paget's disease and molluscum contagiosum.

Jacobaeus<sup>9</sup> in 1904 originated the view that the so-called Paget cell is from the first a malignant cell and that it represents an extension into the epidermis from underlying glandular carcinoma. Cheatle in 1923 and in 1930<sup>10</sup> concluded that changes in the epidermis might result from carcinoma originating in different foci and that the origin must be determined separately in each case.

In 1927 Sir Robert Muir<sup>11</sup> further elaborated the view of Jacobaeus. Through his studies Muir was able to demonstrate that in his material "Paget's disease" was consistently associated with changes in the ducts. These changes varied from hyperplasia to intraductal types of carcinoma. He defined a "Paget cell" as a mammary cancer cell growing within a non-neoplastic epidermis.

#### CLINICAL CHARACTERISTICS

What has been called "Paget's disease of the breast" begins as an intractable eczema of the nipple or areola (fig. 1). The patient's first recollection of the onset is an often recurring pruritis of the skin in this region. Again, the first symptom may be a simple crust associated with weeping or even bleeding of a minor character when it is removed. In some instances the first bleeding is noted to come from the summit of the nipple, though this may not correspond with the center of the cutaneous lesion. In any event the cutaneous lesion fails to respond to treatment with simple ointments or protection from irritating clothing and often alternates for long periods between weeping and drying with crust formation.

9. Jacobaeus, H. C.: Paget's Disease und sein Verhältniss zum Milchdrüsenkarzinom, Virchows Arch. f. path. Anat. **178**:124, 1904.

10. Cheatle, G. L., and Cutler, M.: Tumors of the Breast, Philadelphia, J. B. Lippincott Company, 1930.

11. Muir, R.: Paget's Disease of the Nipple and Its Relationships, J. Path. & Bact. **30**:451-471 (April) 1927.

The ages of the patients studied in this series varied, but all patients were past 30. There was no decade which had a preponderance of the cases, though 22 of the 29 patients were

TABLE 1.—Age Distribution of Patients

Age Periods, Yr.*	Number of Cases
31 to 40.....	3
41 to 50.....	7
51 to 60.....	8
61 to 70.....	7
71 to 75†.....	4

\* The youngest patient was 31 years.

† The oldest patient was 75 years.

between 40 and 70 years when first seen. The duration of the cutaneous lesion before the patient consulted a physician varied within broad limits (table 2), but the preponderance of the

TABLE 2.—Duration of Cutaneous Lesion

	Cases, No.
Less than one month.....	3
One month to one year.....	12
One year to two years.....	6
Two years to three years.....	3
Three years to four years.....	2
Forty years.....	1
Thirty-five years.....	1
Unknown duration.....	1

patients here observed had noted a lesion on the skin for from one to three years previously. Three of the patients had noted a cutaneous manifestation for two weeks, thirty-five years and forty years respectively. The cutaneous lesion when ulcerated is usually bright red and inflamed, with a velvety surface of fine granular material. This may be small, or it may be extensive, with complete destruction of the nipple and involvement of the entire areola and contiguous cutaneous surface.

The patients in some instances complain also of a lump in the breast, though frequently one

TABLE 3.—Mass Palpable in Breast Affected

	Cases, No.	Cases, %
Yes.....	17	59
No.....	12	41

may be discovered which has escaped the notice of the patient. In this series 17 patients (59 per cent) presented a demonstrable breast mass while 12 (41 per cent) had no grossly evident mass (table 3). Clinically, any eczema of the breast should arouse suspicion, and any such lesion which does not completely respond in a period of two weeks to conservative therapy with a





Fig. 1.—A characteristic picture of secondary epidermal carcinoma of the breast ("Paget's disease"). There is seen here thickening of the epidermal layer. In the corium is a capillary network as well as a moderate chronic inflammatory cellular infiltration. There are present in the epidermis abnormal large cells with neoplastic qualities and a surrounding clear zone ( $\times 140$ ).

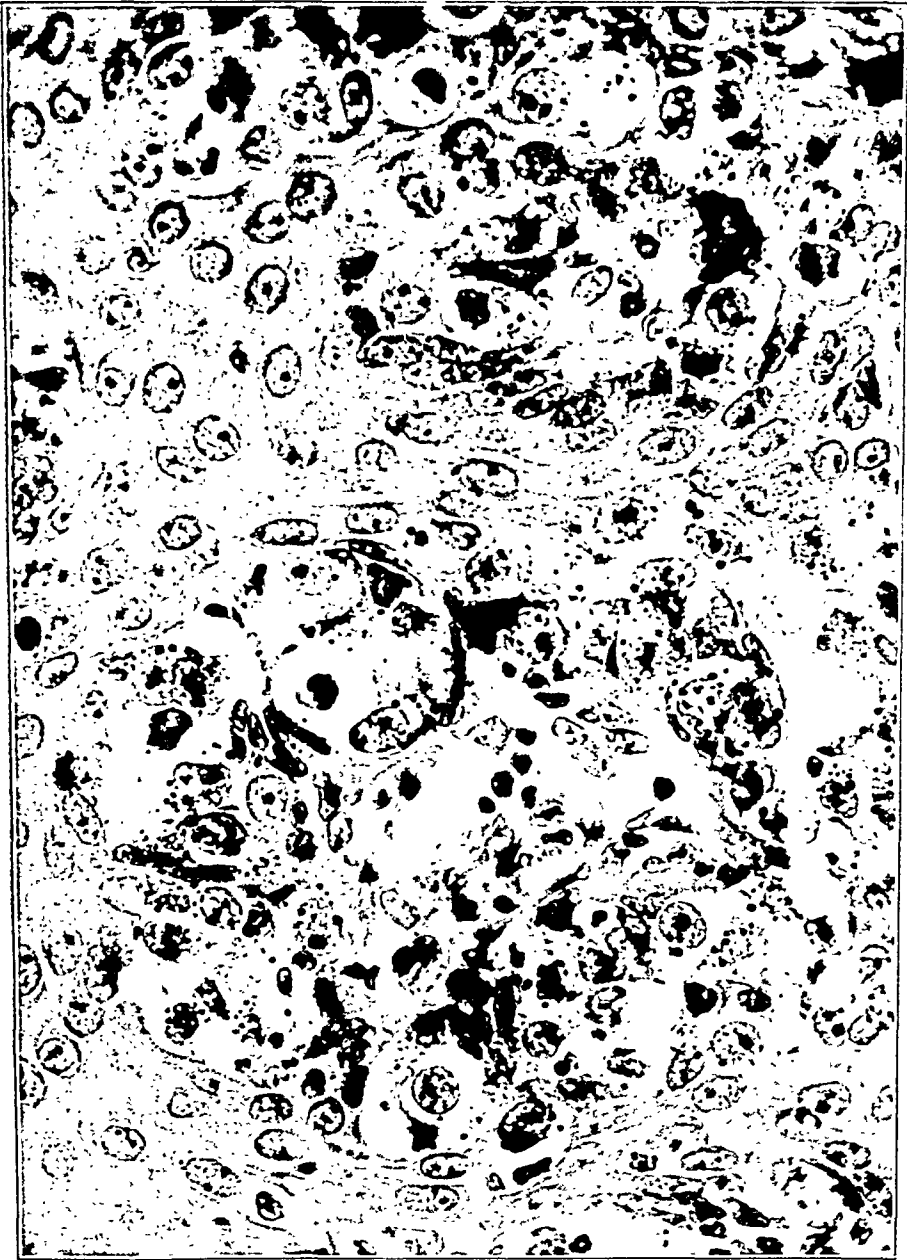


Fig. 2.—A view of the epidermis from a case such as that seen under lower magnification in figure 1 ("Paget's disease"). Here one sees the intraepidermal malignant cells dispersed singly and in bizarre clusters among the epidermal cells. Note that the neoplastic cells ("Paget cells") are generally large and have clear cytoplasm and pyknotic nuclei, and in no instance can be demonstrated intercellular bridges between the abnormal cells and the epidermal cells. The latter characteristic is in favor of the theory that the abnormal cells do not arise in the epidermis. Note also, in this regard, that the contiguous epidermal cells are displaced and compressed by the growth of the neoplastic cells ( $\times 400$ ).

bland ointment and protection from clothing that might be irritating should be subjected to biopsy.

#### PATHOLOGY

The characteristic part of the picture is found in the skin of the breast in the areolar region

most instances, though occasionally it is distorted, destroyed or only partially invaded by the "Paget cells." The corium contains a dense infiltration of lymphocytes and plasma cells as well as a rich supply of tiny capillaries. The

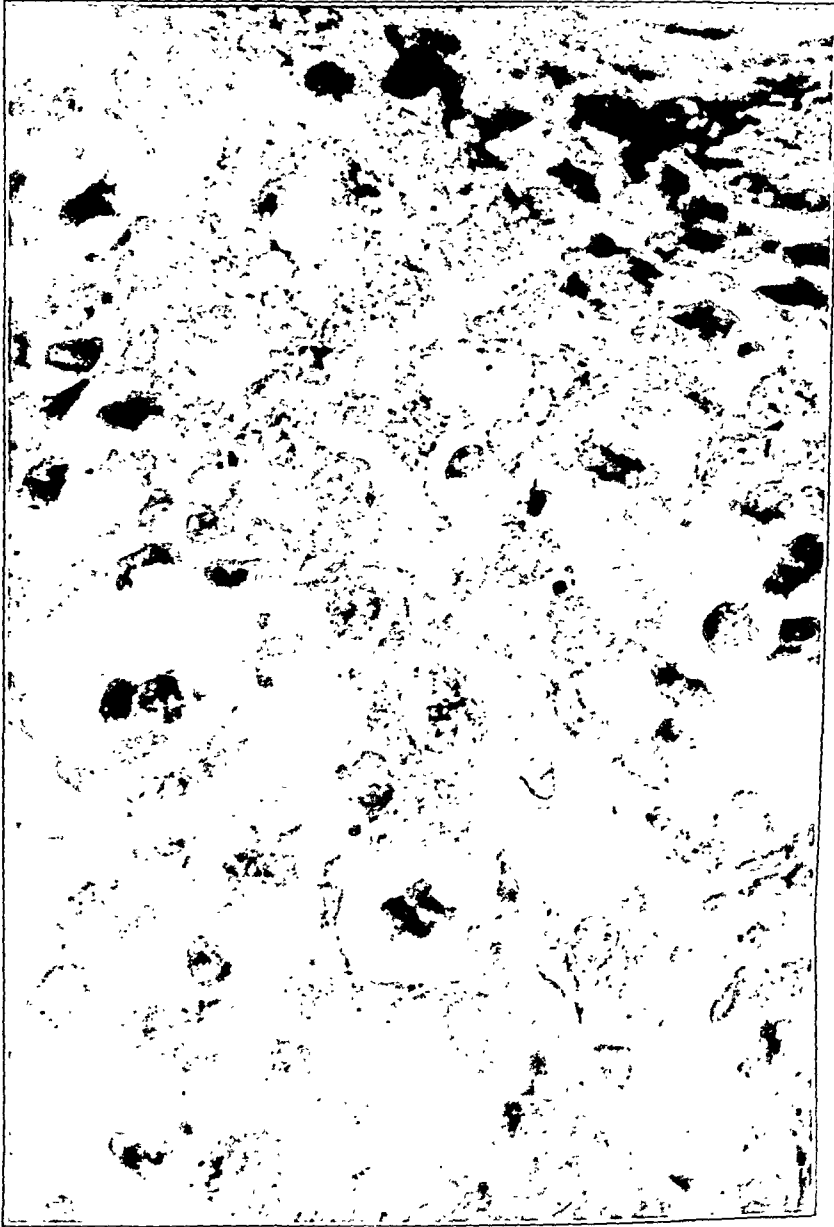


Fig. 3.—A mitotic figure appearing in an intraepidermal metastatic cancer cell ("Paget cell"). Such mitoses and other characteristics of neoplastic cellular patterns are typical of these cells ( $\times 700$ ).

(fig. 2). The malpighian layer is usually thickened, and the rete pegs are elongated and broadened. The basal cell layer remains intact in

most striking and the only consistent and sine qua non feature of this microscopic picture is the presence in the epidermis of a large neo-

lastic cell, the so-called Paget cell. This cell varies in size and other characteristics, just as any neoplastic cell might in any other locus. It is usually round or ovoid. Its nucleus is hyperchromatic, and mitotic figures are occasionally

degeneration (fig. 2). Characteristically, this neoplastic cell is surrounded by a clear space, and in no instance are intercellular bridges found to exist between it and the prickle cells. This picture must be differentiated from (1) Bowen's

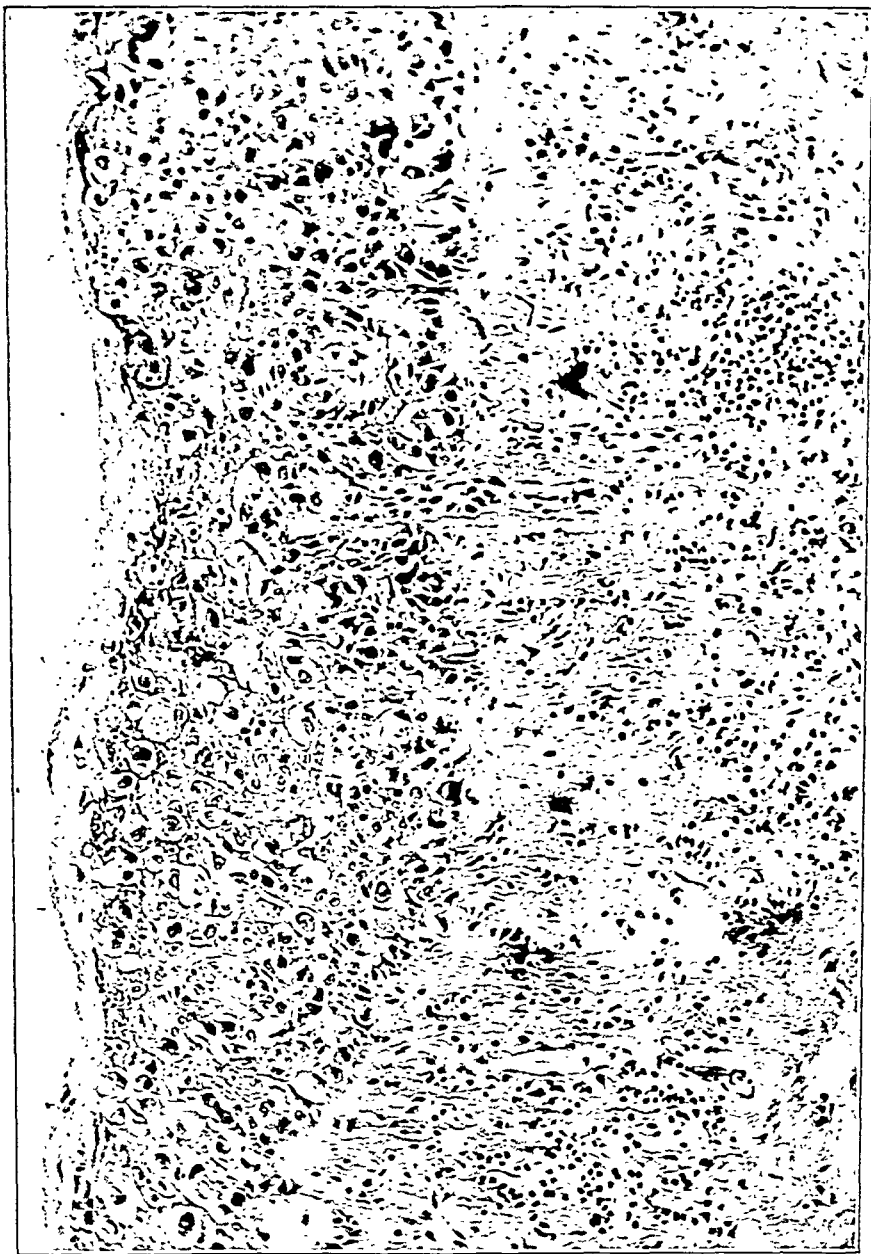


Fig. 4.—Bowen's disease of the skin. Here, again, the characteristic feature of the microscopic picture is the presence in the epidermis of abnormal cells. The Bowen cells, though large, have much intracellular edema and eccentrically located nuclei. Multinucleated cells are common and are spoken of as "basket cells." Hyperkeratosis as seen here is a frequent accompaniment of this lesion, while it is absent in intraepidermal metastasis ("Paget's disease") ( $\times 140$ ).

seen (fig. 3). The cells may occur singly or in bizarre clusters. The adjacent epidermal cells are often distorted by compression or hydropic

disease, (2) superficial epitheliomatosis, (3) simple eczema of the nipple and (4) squamous cell carcinoma of the breast.

1. *Bowen's Disease*.—Certain resemblances exist between Bowen's and "Paget's" diseases (fig. 4). Generally, Bowen's disease is considered to be a primary epithelial malignant growth of low grade and slow progression.<sup>12</sup> The characteristic feature is a large intraepi-

dermal cell. This cell has a vacuolated cytoplasm and a small, deformed, shrunken nucleus, which is displaced to one side.

Also present in the epidermis are larger, multi-nucleated cells, the so-called basket cells. Inter-cellular edema is slight or not present at all in



Fig. 5.—A higher magnification of the epidermis of Bowen's disease. The Bowen cells again present the characteristics of malignant cells (irregular size and shape, pyknotic nuclei and multiple nuclei) although there can be seen intercellular bridges extending between the Bowen cells and the adjacent epidermal cells. This is an indication that the neoplastic cell probably evolved from an epidermal cell. This presence of intercellular bridges can never be found in "Paget's disease," this fact furthering the evidence against the theory that "Paget cells" arise from epidermal cells ( $\times 400$ ).

12. Herold, W. C., and Cooper, Z. K.: Bowen's Disease: An Intra-Epidermal Carcinoma. *S. Clin. North America* 24:1033-1043, (Oct.) 1944.

Bowen's disease, while it is often abundant in "Paget's disease." The chief distinguishing feature is that which would be expected in a cor-

TABLE 4.—Summary of Data in 29 Cases of Cancer of the Breast

Case No.	Age, Yr.	Duration of Cutaneous Lesion	Palpable Mass	Clinical Picture	Pathology	Course
1	45	2 yr.	Yes	Two years ago patient taped both nipples with adhesive tape; right nipple became irritated and has refused to heal; nipple discharges serum and has been seat of constant pruritus; lump descended in right breast many years ago; no bleeding; bleeding surface; 2 in. (5 cm.) above right nipple is indolent 1 in. (2.5 cm.) nodule; no nodes palpable	Adenocarcinoma of breast, with continuity of carcinoma cells in dermis into epidermis; in addition to intradermal extensions, ulceration and chronic inflammatory reaction found	Cutaneous lesion treated with petrolatum dressing for 6 wk.; with no improvement; 10/9/29, radical mastectomy performed; 9/22/31, no recurrence demonstrable
2	50	?	No	Patient's mother had carcinoma of the breast; patient rescued by kitten; pruritic and bleeding lesion ensued; no response to treatment with ointment; 40 per cent areola ulcerated and crusted; no nodes palpable	Intraductal carcinoma and intradermal malignant cells (Paget); no metastasis to lymph nodes	Biopsy of nipple revealed "Paget's disease"; 11/29/34, radical mastectomy performed; 9/15/41, no recurrence demonstrable
3	51	3 wk.	Yes	Patient aware of lump in left breast for 30 yr.; 3 wk. ago small ulcer developed at apex of left nipple, with no bleeding from lesion or nipple; nipple is verrucous, with crusted, 8 cm. ulcer; palpable mass deep in outer lower quadrant, which is not attached to the skin	Adenocarcinoma of breast and intradermal metastasis (Paget's disease of the skin)	10/20/37, simple mastectomy performed, physician believing patient had "cystic disease and keratosis of nipple"; 12/3/37, radical excision of remainder completed; 11/22/41, no recurrence found
4	61	1 yr.	No	Patient noted crusted lesion at tip of left nipple for 1 yr.; "gradually becoming worse"; Examination: Reveals such a lesion measuring 4 sq. cm.	(1) Typical "Paget's disease of nipple"; (2) adenocarcinoma of breast, with extensive axillary metastases	(1) 7/30/37, lesion and entire nipple excised; 3/18/38, 3 cm. hard mass in axilla and 1 cm. soft nodule in left axilla discovered; (2) 4/1/39, radical mastectomy performed on left side; 11/11/40, patient died from generalized carcinomatosis
5	70	3 yr.	No	For 3 yr. patient had pruritus and burning of right nipple, also ulceration of nipple, with periods of healing Examination: Nipple eroded away by 6 cm. ulcer; no nodes palpable	Intraductal carcinoma; duct lined with malignant cells extends to skin of nipple and becomes continuous with intradermal invasion by malignant "Paget" cells	Simple mastectomy performed (because of patient's age) 7/13/33; 3/17/33, no recurrence
6	61	1 yr.	Yes	One year ago patient observed skin of left nipple "peeling off"; this continued, with no pain or discharge Examination: 2 cm. soft, pink excoriated left nipple; deep in breast tissue in upper outer quadrant is 3 by 1 cm. irregular mass	Biopsy reveals typical intradermal malignant cells, with intact basal cell layer; ductal carcinoma in underlying breast ducts	7/28/35, radical mastectomy performed on left side
7	40	0 mo.	Yes	Exuding ulcer of left breast present for 0 mo Examination: Superficial erosion of left nipple; subjacent to nipple is irregular hard mass fixed to the skin; hard, movable nodule palpable in left axilla	Adenocarcinoma of breast and at epidermal margin, adenocarcinoma extensions; also in these zones are intradermal extensions of same cells, yielding the typical picture of "Paget's disease"	8/11/44, radical mastectomy performed; 12/6/44, no evidence of recurrence
8	46	20 mo.	Yes	Patient discovered irritation and pain around right nipple 20 mo. ago; some bloody discharge associated with this Examination: Half of nipple excoriated and granulating; hard fixed subjacent mass palpable in breast	Adenocarcinoma of breast in continuity with epidermal picture of "Paget's disease"; some extensions of malignant cells can be traced into epidermis, in which they appear as "Paget cells"—actually malignant cells	12/3/39, radical mastectomy performed; no recurrence found when patient was last seen, 4/19/40
9	49	5 mo.	Yes	Five months ago patient noted her clothing adhering to left nipple; crust formed, with occasional bloody discharge; small lump noted at same time, which has increased slightly in size Examination: 7 cm. crusted ulcer on left nipple; subjacent to it is 1 cm. mass; 1 cm. hard nodule palpable in left axilla	Adenocarcinoma of breast with lymph node metastases; nipple lesion presents typical picture described as "Paget's disease" with resemblance of "Paget cells" to carcinoma cells of breast	8/9/40, radical mastectomy performed on left side; in 1942 patient died of hypertension
10	46	8 wk.	No	Eight weeks ago patient noted small red spot on left nipple; has had some pruritus	Adenocarcinoma of left breast and changes characteristic of "Paget's disease" in skin of nipple	12/30/40, simple mastectomy performed on left side; 12/30/42, no recurrence; patient not seen since

TABLE 4.—Summary of Data in 29 Cases of Cancer of the Breast—Continued

11	47	3 mo.	No	Three months ago patient noted small ulcer on right nipple; failed to improve with application of ointment at home	Adenocarcinoma of breast and no disturbance in basal layer of the epidermis; however, intra-epidermal cells of "Paget" are typical malignant cells similar to those of the cancer of breast	11/8/10, radical mastectomy performed on right side; 0/10/11, no recurrence
12	48	2 yr.	Yes	Two years ago patient noted pruritus and small red "hump" on right nipple; subsequently, similar nodules appeared in skin of breast and have progressively grown larger Examination: Skin of right breast involved with multiple small, hard nodes as far as the midline anteriorly and posteriorly; large, hard mass at nipple, with surface crater, palpable	Adenocarcinoma of breast and intraepidermal cell clusters of malignant cells	4/5/17, shoulder girdle amputation and radical mastectomy performed; 4/9/17, patient died
13	60	3 yr.	Yes	Three years ago patient noted pruritus and crusting of right nipple; 3 mo. ago she noted lump in right breast Examination: Vagely 2 cm. superficial ulceration of right nipple concentric with nipple; no definite mass discernible in breast by examining physicians	Adenocarcinoma of right breast with axillary metastases; changes in skin of nipple are typical of "Paget's disease," i. e., intraepidermal secondary malignant cell deposits	5/9/11, radical mastectomy performed on right side; 11/1/12, no recurrence evident
14	62	6 mo.	No	Small superficial ulcer on right nipple noted for 6 mo.; intermittent bleeding from nipple observed for same duration	On multiple sectioning of right breast, in upper inner quadrant was found 2 cm. hard mass; microscopic examination reveals adenocarcinoma with axillary metastases; nipple skin reveals picture of "Paget's disease," and intraepidermal cells appear to be malignant cells which have invaded epidermis	7/25/14, radical mastectomy performed on right side; 9/10/14, no recurrence evident
15	37	2 yr.	No	Two years ago discharge from left nipple developed; crust formed; when it separated, it left an ulcer, which later gradually enlarged; a few months ago tiny bumps formed over skin of breast; all lesions pruritic; no mass in breast and no palpable nodes in axilla	Adenocarcinoma and axillary metastases; lymphatics of dermis filled with adenocarcinoma; varying stages of extensions into epidermis; in other portions are intraepidermal clusters and single malignant cells; typical "Paget's disease of the skin"	1/21/18, radical mastectomy performed on left side; no follow-up
16	71	35 yr.	Yes	Patient has had eczematous lesion of right nipple for 35 yr.; nodule noted in right breast 1 yr. ago; it has slowly enlarged Examination: Superficial ulcer of entire right breast, with 3 cm. palpable mass in breast and palpable node in axilla	Biopsy 10/13/44; typical "Paget's disease of the nipple," with intraepidermal malignant cell invasion	Patient refused operation; 10,000 units of roentgen radiation given to tumor, after which entire process cleared; no mass and no eczema; in 4 mo., eczema reappeared and was more extensive; biopsy repeated; 12/26/45, patient died from carcinoma of the breast
17	42	1 yr.	Yes	Four years ago patient squeezed wartlike excrescence from left nipple; 3 yr. ago she noted exudative lesion on that nipple Examination: Superficial ulcer of nipple and areola and 5 cm. mass movable in outer lower quadrant	Firm tissue deep to nipple contains duct carcinoma; in one section duct with carcinoma can be traced to epidermis; continued into epidermis by malignant invasion; also dermal invasion	11/11/12, radical mastectomy performed; 11/29/14, no recurrence demonstrable
18	53	1 yr.	Yes	One year ago patient noted sore on left nipple, which altered a few days of healing and broke down, with discharge; 9 mo. ago lump to left of nipple noticed Examination: Left nipple retracted, broadened and superficially ulcerated; mass 1 by 3 cm. to left of nipple palpable but not fixed to skin or wall of chest	Adenocarcinoma of breast, with changes in skin characteristic of "Paget's disease"; again intra-epidermal cells present characteristics of neoplastic cells in benign epidermis	2/25/44, radical mastectomy performed on left side; 11/17/44, patient died of generalized carcinoma
19	62	10 yr.	No	Patient noted small bleb on left nipple 10 yr. ago, which 4 yr. ago began enlarging Examination: Two shallow ulcers on left areola; no mass or palpable nodes present	Intraductal carcinoma with intraepidermal malignant cells identical with those in the duct neoplasm in typical "Paget's disease of the skin"	4/16/44, radical mastectomy performed; no follow-up
20	64	11 mo.	Yes	Patient had radical mastectomy of left breast in 1925 for carcinoma; pruritus and recurring scaling of right breast present for 11 mo. Examination: Nipple absent, and areola white, indurated and depressed; nodule palpable just under areola in breast	Adenocarcinoma of breast; typical "Paget's disease of nipple skin"	12/6/37, radical mastectomy performed; no follow-up

TABLE 4.—Summary of Data in 29 Cases of Cancer of the Breast—Continued

Case	Age, Yr.	Duration of Cutaneous Lesion	Palpable Mass	Clinical Picture	Pathology	Course
21	31	2 yr.	No	Pruritus of right nipple present for 2 yr.; in recent months small, extending ulcer of nipple developed, with occasional bleeding Examination: Excoriation, with serous sanguinous weeping of nipple; no mass or palpable nodes discernible	Intraductal carcinoma; in one focus can be seen invasion through wall of a duct; typical "Paget's disease of skin," with close resemblance of intra-epidermal and intraductal malignant cells	6/7/11, radical mastectomy performed on left side; 1/30/15, no evidence of recurrence
22	69	18 mo.	No	For 18 mo. patient noted chapping and crusting of right nipple with pruritus; slow enlargement of lesion Examination: 6 mm. superficial ulcer of right nipple, with induration of entire nipple; no palpable mass found; two small, movable nodes present in each axilla	Adenocarcinoma with lymph node metastases; sections demonstrate nests of adenocarcinoma at basal cell layer of epidermis, with "Paget cells" in adjacent epidermis—identical with carcinoma cells; also lymphatics in derma containing carcinoma cells	6/5/13, radical mastectomy performed on right side; 2/2/15, no recurrence found
23	69	3 yr.	Yes	Three years ago patient noted white film over right nipple, with a pinhead hole in its center; crust and discharge followed, and slowly nipple eroded away; 1 mo. ago patient noted mass in upper part of breast Examination: 8 cm. mass, movable in upper part of breast; nipple is eroded away, with replacement by dirty ulcer	In some sections are adenocarcinomatous arrangements in dermis extending to basal cell layer; in others is direct extension into epidermis; duct also seen, lined with malignant epithelium; these cells identical with intraepidermal malignant cells ("Paget")	5/1/11, simple mastectomy performed; 11/23/11, patient died at city sanatorium with a "psoriasis"
24	78	3 wk.	Yes	In 1929, patient had mastectomy and axillary dissection on right for carcinoma of breast; 10 mo. ago lump noted in left breast and left axilla; for 3 wk. soreness and crusting of left nipple noted Examination: Left nipple enlarged, ulcerated and crusted; 5 cm. hard mass palpable in lower outer quadrant of left breast, and four hard nodes found in left axilla	Breast, adenocarcinoma and "Paget's disease of skin"	5/27/11, axillary dissection and radical mastectomy performed on left side; 7/30/11, lump in right axilla; 8/1/11, axillary dissection performed on right side
25	63	6 mo.	Yes	Small excoriation on right nipple noted 6 mo. before, which alternated with crusting and oozing serum; discharge from nipple for 2 mo. Examination: 3 by 4 cm. ulcer of right nipple, with sharp margins, seen; retraction of nipple pronounced	Deep to the ulcer is 2 cm. mass containing ductal carcinoma; in one section is duct lined with malignant cells identical with "Paget's cells" seen in adjacent epidermis	2/12/23, simple mastectomy performed on right side
26	32	2 yr.	Yes	Left radical mastectomy performed 10 yr. ago for carcinoma; white discharge from right nipple, with crusting of skin, present for 2 yr.; patient noted mass in right breast 2 wk. ago Examination: Retracted right nipple, with white discharge and crusting of nipple skin; 2 cm. mass present in upper outer breast quadrant; it is not attached to the skin; hard mass palpable in right axilla	An adenocarcinoma with axillary metastases; changes in skin typical of "Paget's disease"; in one section is duct filled with malignant cells, and at ampulla the continuity of extension of duct neoplasm with that of epidermis can be traced as they are seen to invade the epidermis at the margin of the ampulla epithelium	7/7/33, radical mastectomy performed on right side; 11/2/11, small shot-dart node present in right side of neck; intratable headaches, vomiting and progressive paralysis of right arm developed; 1/10/12, patient died
27	50	4 wk.	Yes	Small lump in each breast present for 4 wk. Examination: Each nipple retracted, with leathery mass subjacent to and attached to nipple	Adenocarcinoma in each breast; in the skin is typical picture of "Paget's disease"; malignant cells found in the dermis, extending into the epidermis; also in epidermis are multiple epidermal cells in state of hydropic degeneration	12/23/11, bilateral simple mastectomy performed; no follow-up
28	63	?	Yes	Mass in right breast noted 1 yr. ago; gradually increased to about three times its original size Examination: Retraction of skin of nipple; an orange-sized mass in outer lower quadrant of right breast attached to skin	Adenocarcinoma of breast, with extension into all layers of skin and ulceration in one zone; in margins of ulcerated zone are two abnormal cell types in epidermis; epidermal cells with hydropic degeneration and malignant cells identical with those in corium and breast tissue; latter are characteristic "Paget cells"	10/27/31, right radical mastectomy performed; 9/5/32, patient died of undetermined cause
29	68	6 mo.	No	Beczema-like eruption around right nipple present 6 mo. and failed to heat or improve with applications of ointments	Ductal carcinoma of the breast found, and some ducts filled with carcinoma cells traced to the epidermis, in which was a typical intraepidermal metastasis (Paget's disease)	5/11/15, simple mastectomy performed



sideration of the two different processes involved in pathogenesis. This is that in "Paget's disease" there is actual dissociation of the abnormal cell, whereas in Bowen's disease the cell continuity with adjacent epidermal cells is retained

2. *Superficial Epitheliomatosis*.— Superficial epitheliomatosis<sup>13</sup> may be of squamous cell or basal cell origin or mixed in character. It differs from the ordinary primary epidermal malignant neoplasm in that the malignant invasion extends



Fig. 6.—Chronic eczema. Here the picture is obviously one of chronic inflammation without any evidence of malignancy. Note the characteristic features: vesicle formation on the epidermal surface, interstitial edema, chronic inflammatory infiltration, parakeratosis and acanthosis ( $\times 140$ ).

and the intercellular bridges in the rete malpighii are preserved (fig. 5). Hyperkeratosis is frequently seen in Bowen's disease, while it is absent in "Paget's disease."

upward into the epidermis from the basal cell zone rather than down into the dermis. Here,

13. Montgomery, H.: Superficial Epitheliomatosis, Arch. Dermat. & Syph. 20:339-357 (Sept.) 1929.

en, is an intraepidermal carcinoma which is primary, as opposed to the "Paget" type of change, which is secondary. In the former, all the characteristics of the primary carcinoma are present and intercellular bridges may be found.

3. *Simple Eczema*.—In simple eczema the microscopic changes in the epidermis are ob-

perplasia, desquamation, edema and hydropic degeneration of epidermal cells.

One finds vesicle formation on the surface, parakeratosis (nucleation of cells in the exfoliative layer), acanthosis (thickening of the epidermis), interstitial edema and chronic inflammatory cell infiltration.



Fig. 7.—Intraepidermal metastatic carcinoma ("Paget's disease") resulting from extension by continuity of adenocarcinoma from underlying breast. Here one can see carcinoma cells arranged in strands filling interstices and lymphatics of the corium. At some points invasion through the basal layer into the epidermis can be seen, and in the layers of the epidermis are seen changes typical of "Paget's disease." These abnormal intraepidermal cells are identical in detail with the carcinoma cells found in the corium and the breast tissue ( $\times 140$ ).

viously not those of malignant processes (fig. 6). The basis of the process is inflammation, with secondary epidermal changes resulting from hy-

4. *Squamous Carcinoma*.—Of the 1,430 radical mastectomies performed at Barnard Hospital for carcinoma of the breast, in only 3 were there



Fig. 8.—Breast duct carcinoma extending to the nipple surface. Here one sees a typical ductal carcinoma. The carcinoma-filled duct is traced to the nipple in which there is encountered an ulceration and chronic inflammatory cell reaction. At the epidermal margin adjacent to the surface ulcer is found a typical section of epidermal carcinoma ("Paget's disease") illustrated in figure 9. Thus is demonstrated metastasis to the epidermis from a breast carcinoma by extension along a duct ( $\times 75$ ).



Fig. 9.—Secondary epidermal carcinoma ("Paget's disease") resulting from extension along a duct of a primary duct carcinoma of the breast. This section was taken from the margin of the ulcer seen in figure 8 and demonstrates the intraepidermal carcinoma cells identical with the duct carcinoma cells ( $\times 150$ ).

squamous cell carcinomas and 1 of these was in a man. In each instance the lesion was in the upper outer quadrant of the breast skin, well away from the region of the areola and nipple.

Squamous cell carcinoma presents little difficulty in differential diagnosis. The malignant invasion into the dermis of sheets of cells, the pearl formation and other characteristics of squamous cell malignancy are absent in "Paget's disease." The occasional case of "Paget's" cutaneous change associated with complete destruction of the basal layer may offer some difficulty, but the features of cell dissociation and absence of bridges prove the picture of "Paget's disease."

#### RESULTS IN A STUDY OF TWENTY-NINE CASES

The clinical course of these patients has been followed, and the skin and the glandular and stromal elements of the underlying breasts were studied pathologically. The findings in these 29 cases support the view of Jacobaeus and Muir, viz., the "Paget cell" is a malignant cell growing in a non-neoplastic epidermis. These cases demonstrate:

1. That adenocarcinoma of the breast was present in every case in which the diagnosis of "Paget's disease of the breast" was made histologically.
2. That the intraepidermal cell called "Paget cell" presents the identical histologic picture of the cancer cells found in the underlying carcinoma of the breast.
3. That the intraepidermal cancer cells extend into this locus in various manners. In some, continuity is traced from the breast carcinoma through lymphatics in the subcutaneous tissue and the corium (fig. 7); in others there is found direct extension along the interstices, and in still others one sees direct extension of malignant cells from ducts of the breast into the epidermis at their junction (fig. 8).

In some of my cases it has not been possible to demonstrate continuity of spread by any of these channels. However, I cannot but be of the opinion that it could be revealed in each case were adequate serial sections taken with this purpose in view.

4. That the changes in the skin of the breast also attest to this chain of events in their development. The intraepidermal clusters of cells sometimes present an acinar arrangement. The contiguous epidermal cells are usually distorted secondarily by compression or by hydropic degeneration, and in no instance do the epidermal cells present any gradation of changes ranging from normal to malignant. In no instance can

intercellular bridges be demonstrated between the epidermal cells and the malignant cells, and in no instance does the epidermal cell show any tendency toward epidermal reproduction, such as might be expected in a primary epidermal malignancy.

#### NATURE OF THE MALIGNANT LESION OF THE BREAST

In this series of cases, there was nothing unusual in the type of breast cancer associated with the cutaneous manifestation. However, one interesting phenomenon was observed, which probably explains why the cutaneous lesion in some instances has existed for a long period before frank carcinoma of the breast could be recognized clinically. In some cases extremely early intraductal carcinoma was present, which had become quarantined by fibrous tissue before it became very large. This, plus its position immediately beneath the nipple, made it impossible to be palpated and limited its growth. It is this type of cancer that is more likely to go undiscovered by incomplete pathologic examination, and it is this same type that presents in a high frequency of cases no palpable mass. This intraductal type of carcinoma may be confused with benign lesions showing a pronounced degree of hyperplasia. However, on closer examination, one can discover areas at which the malignant cells have already broken through the elastica and have begun periductal infiltration. Just how long such a lesion may exist before it assumes this last characteristic, periductal invasion, is a matter of conjecture. Probably it varies. But in any event it is the most likely explanation for the existence of malignant cells in the epidermis for long intervals before frank carcinomatous masses appear in the breast proper. Apparently the malignant process in the duct may extend to the epidermis along the course of the duct and present a dermal and epidermal lesion long before actual invasion of an extensive nature occurs in other directions. On the other hand, there is adequate evidence that such an apparently trivial lesion may have metastasized at this early stage to the axillary lymphatics. It is for these reasons that the emphasis must be placed on early radical therapy irrespective of the presence of a palpable mass or of the duration of the cutaneous lesion. The fact that the cutaneous lesion has been present for a long period does not by any means preclude the fact that the patient also has microscopic evidence of cancer of the breast and even axillary metastases. Still, in the majority of the cases, a frank adenocarcinoma was present and it was impossible to ascertain

whether it originated in acinar or duct cells. In only 8 of the 29 cases in this series was there an intraductal carcinoma.

#### EXTRAMAMMARY "PAGET'S DISEASE"

In 1937 H. A. Weiner<sup>14</sup> reviewed the 57 cases which until that time had been reported as instances of "extramammary Paget's disease." He so presented the details of a case of his own. In his patient, he too was able to demonstrate that the intraepidermal cells were, in truth, neoplastic cells extending from a subjacent apocrine gland carcinoma of the vulva. Following a critical study, he concluded that only 15 of the 57 cases so reported entailed sufficient evidence (microscopic examination) to warrant such a diagnosis. In all the acceptable cases the changes occurred in the skin of the areas (axilla and anogenital regions) in which the apocrine sweat glands are present. Of these 15 cases, 9 presented definite evidence of carcinoma elsewhere than in the epidermis, and this in each instance was a glandular carcinoma. In the remaining 6 cases, either no mention was made of cancer or no adequate examination to discover its presence was performed. Others have reported intraepidermal metastatic carcinoma associated with epithelioma, melanoma and rectal carcinoma. Such an observation has led Drake and Whitfield and Civatte (cited by Weiner) to propose that "Paget's disease of the skin" is a nevocarcinoma.<sup>15</sup> Actually, however, a variety of tumors have produced the phenomenon, and it is unreasonable to postulate that all such metastases must be explained on the basis of one particular type.

#### COMMENT

From the evidence obtainable some tenable conclusions may be drawn:

1. Intraepidermal metastatic carcinoma has been repeatedly seen as an accompaniment of

14. Weiner, H. A.: Paget's Disease of the Skin and Its Relation to Carcinoma of the Apocrine Sweat Glands, *Am. J. Cancer* **31**:373-403 (Nov.) 1937.

15. The intraepidermal presence of *thèques* and clear cells in junction type nevi and in melanomas has been repeatedly observed. The clear cell of the junction nevus is easily differentiated from the "Paget cell." Opinion varies here, again, as to the nature of this intraepidermal cell, though from the evidence at hand it appears that the cell originates in the epidermal layer and does not represent an invasion into it. (Becker, S. W.: Cutaneous Melanoma: A Histologic Study, Especially Directed Toward the Study of Melanoblasts, *Arch. Dermat. & Syph.* **21**:818-835 [May] 1930. Nicolau, S.: Sur le phénomène de migration cellulaire intra-épidermique dans le névocarcinome, *Ann. de dermat. et syph.* **1**:746-762 [July] 1930. Traub, E., and Keil, H.: The "Common Mole." *Arch. Dermat. & Syph.* **41**:214-252 [Feb.] 1940.)

various types of malignant disease variously situated. Some of these metastases have been demonstrated as occurring by variable routes, viz., direct extension, ductal extension or by way of lymphatic channels.

2. The inaccuracy of explaining all such intraepidermal metastatic malignant growths on the basis of a single type of carcinoma is evident, since they may occur from underlying breast carcinoma, from epithelioma, from melanoma, from apocrine gland carcinoma and possibly from others.

3. Much of the difficulty which has arisen in regard to this picture is the result of eponymic labeling of the disease. While due credit should be attributed to Sir James Paget for first calling attention to the relationship between carcinoma of the breast and an eczema-like lesion of the nipple, the term "Paget's disease" has proved unfortunate because it has defeated the very purpose of illustrating this relationship. The placing of all such lesions into a group and labeling them "Paget's disease" has confused not only the clinician who desires to know what he is treating in order that he may treat it adequately but also the pathologist who attempts to theorize on the basis of 1 or several cases as to the nature of what he believes must be an entity, "Paget's disease."

One purpose back of the presentation of this study is to recommend that the terms "Paget's disease of the breast" and "extramammary Paget's disease" be abandoned altogether. The fact that the cells called "Paget cells" are carcinoma cells has been established. No typical and acceptable case of "Paget's disease" which has been adequately studied can be found that is not associated with carcinoma. It is essential to the welfare of such patients, then, that their maladies be recognized as cancer at the earliest possible stage, that is, when the cells are seen in the skin and not when the patient returns with obvious progression following inadequate treatment. When carcinoma cells are discovered in a benign epidermis, they should be called carcinoma cells rather than "Paget cells." In the case of breast lesions, the clinician could and should then treat the malady as a carcinoma primary in the breast, irrespective of palpable mass. In 41 per cent of 29 cases there was no palpable mass when the diagnosis of the skin was made, and yet adenocarcinoma of the breast was demonstrated microscopically. Thus, earlier recognition and earlier treatment of carcinoma in such cases will result.

## SUMMARY

1. "Paget cells" appear to be metastatic cancer cells.
2. In order to insure earlier recognition, refractory eczematoid lesions of the breast should be subjected to biopsy.
3. The origin of "Paget cells" may be from breast carcinoma, epithelioma, rectal adenocarcinoma, apocrine sweat gland carcinoma or other tumors.
4. The mode of extension may be by direct extension, retrograde lymphatic continuity or ductal spread.
5. Twenty-nine cases of "Paget's disease of the breast" are presented to attest to these facts.
6. In order to reduce confusion among pathologists and clinicians and in order to facilitate earlier and more rational therapy, the eponymic nomenclature ("Paget's disease of the breast" and "extramammary Paget's disease") should be abandoned.
7. "Secondary epidermal carcinoma" is suggested as a preferable term.
8. Treatment of secondary epidermal carcinoma must proceed along the lines of rational elimination of the primary carcinoma as well as of the cutaneous lesion.
9. In order to insure higher curability rate, treatment for secondary epidermal carcinoma of the breast must include radical mastectomy, whether the primary site can be palpably detected or not.

# SKELETAL FIXATION OF MANDIBULAR FRACTURES

REPORT OF FIVE CASES, WITH NINE FRACTURES

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AND

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DIXON, ILL.

Injuries to the head have been steadily increasing in the past quarter of a century, and fractures of the mandible in particular have increased manifold. The illustration (fig. 1) from Fomon's textbook<sup>1</sup> shows the various sites of fractures and the frequency of occurrence. While this is an accurate and standard chart, the present situation presents a more complex picture. The forces causing head injuries seem to be more intense, with the result that the fractures are frequently multiple and the displacement of the fragments extremely complicating.

Broken jaws have been recorded in medical history since 3,000 B. C., according to Breas-

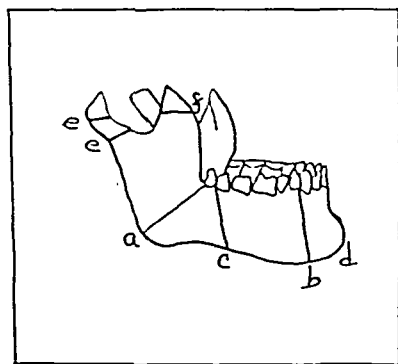


Fig. 1.—Sites of predilection of mandibular fractures, in order of frequency: (a) angle; (b) mental foramen; (c) molar region; (d) symphysis; (e) condyle and (f) coronoid process. (From Fomon.<sup>1</sup>)

ted's<sup>2</sup> translation of the Edwin Smith surgical papyrus. Since this recording of such an injury, there have been numerous methods of treatment. We have tried many of these with varying degrees of success. Until the advent of skeletal fixation, there has not been a universal method of treat-

ment adequate to handle any fracture that was presented. It is still possible for the condyle to be broken so short that pins cannot be inserted. In such a rare instance, an open operation would be mandatory.

Because of the increasing frequency of injuries to the head with the resulting fractures of the mandible and the superior maxilla, we feel that each locality or each hospital should have a group which is interested in such fractures. The ideal team is an oral surgeon, an otolaryngologist and a general surgeon. The oral surgeon contributes his knowledge of the alinement of the teeth and the methods of securing a functioning bite. The otolaryngologist contributes his knowledge of the bones of the face and his ability to handle other fractures of the face as well as other complicating injuries of the head and neck. The general surgeon, with a large practice in fractures, advises as to the alinement of the teeth and the general condition of the patient.

Roger Anderson<sup>3</sup> has been credited with the practical development of the treatment of fractures by external appliance and pin fixation. This is the apparatus that we used. There are other appliances on the market, but we decided to use this because of its simplicity and light weight. It is simple, safe, comfortable and economical.

Gillies<sup>4</sup> listed the advantages of external skeletal fixation: 1. It is available for types of fractures which cannot be treated by other methods. 2. It may be immediately applied to any fracture. There is perfect control of all fragments and anatomic reposition. 3. It permits immediate movement of the temporomandibular joint. 4. It provides for cleanliness of the whole buccal cavity. We found all these advantages, and so far we have found no disadvantages.

We have seen roentgenograms of other patients, in whom the pins were placed too high.

1. Fomon, S.: *Surgery of Injury and Plastic Repair*, Baltimore, Williams & Wilkins Company, 1939, p. 1203.

2. Breasted, J. H.: *Edwin Smith Surgical Papyrus*, Published in Facsimile and Hieroglyphic Transliteration with Translation and Commentary, Chicago, University of Chicago Press, 1930.

3. Anderson, R.: *Ambulatory Method of Treating Fractures of Shaft of Femur*, Surg., Gynec. & Obst. **62**:865-873 (May) 1936.

4. Gillies, H. D.: *Replacement and Control of Maxilla Facial Fracture*, Brit. Dent. J. **71**:351-358 (Dec.) 1941.



They were in the loose tissue of the alveolar process and at various angles. If good results are to be obtained, the apparatus must be applied correctly. Waldron<sup>5</sup> has told how to place the pins:

The pins are inserted through the skin without incisions and through the mandible about 5 mm. above the lower border. The pins are placed at an angle of approximately 70 degrees and a hand drill is recommended for their insertion. The pin clamps are then applied and connected by a rod, and thus a strong and secure fixation of the fragment is assured. A second unit is placed in the adjacent fragment. The displacement is then reduced manually and the fracture immobilized by joining the two units by means of two universal fixation rod clamps and a fixation bar. This appliance can be loosened and adjustments made in the event complete reduction and proper alignment have not been secured at the time that it was first employed.

We are enthusiastic about this skeletal fixation. All of our pins have been well placed, and healing and occlusion have been excellent. We recommend wholeheartedly that before the first attempt at pinning condylar fragments one go to the laboratory. One should place the pins in the attached condyle and then make a window and observe where the pins are placed. Through a skin flap, the condyle on the opposite side should be severed from the mandible with a Gigli saw at the point of fracture in the patient to be operated on. Then after the skin flap has been replaced, the pins should be placed in this fragment. Thoma<sup>6</sup> used only one pin in the short fragment, but we prefer two. By placing two pins in the fragment, we have absolute fixation at once and the patient has all motions of his jaw.

All the patients in the following cases, with 1 exception, had their fractures reduced and skeletal fixation applied while they were under pentothal sodium anesthesia. The operating time, which included taking of roentgenograms for checking alinement, varied from forty minutes in the cases of angle fracture to three hours and forty minutes in case no. 5, with the multiple fractures.

#### REPORT OF CASES

**CASE 1 (figs. 2 and 3).—**A pullman porter, aged 63, was critically injured in a train wreck. Head injuries included a basal skull fracture and two fractures of the inferior maxilla, with the symphysis floating free and with pronounced displacement of the lower fragment. The patient was edentulous. His condition was further complicated by severe burns on his neck extending to the lower border of the inferior maxilla. The burned area

was infected; thus an open operation could not be considered. The general condition of the patient, which included additional fractures and burns, delayed the setting of the jaw two and a half weeks.

Owing to the callus formation, perfect alinement of the fragments was impossible. However, the end result was so good that dentures could be installed within three weeks after the immobilization of the fragments, at which time the patient could properly masticate solid food. Registration of the bite was obtained by McGrane's pin tracer technic. Immediately after the immobilization of the fragments with the skeletal fixation, the patient's mental haziness cleared. Food could be utilized, and the immediate improvement was evidenced in physical as well as mental well-being. The

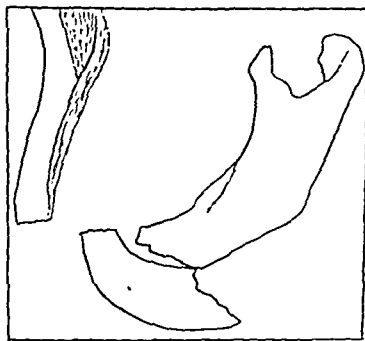


Fig. 2.—Diagrammatic drawing showing the symphysis floating free and overriding.

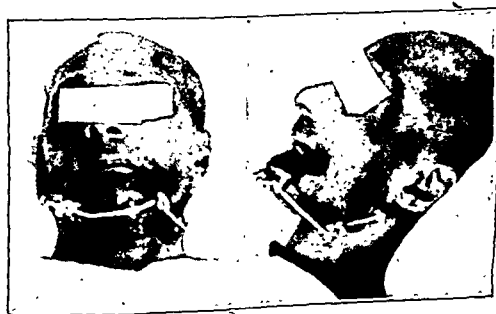


Fig. 3.—Firm and permanent fixation of the symphysis.

change effected in such a case is so pronounced that one must see it to appreciate it. The pins were removed at the end of eight weeks.

Cases 2 and 3 were instances of fracture of the angle of the jaw with the third molar loose and in the crevice of the fracture holding these ends apart. These angle fractures are the easiest of all to immobilize and aline with exterior fixation, but they present an unsolvable problem for any other method.

**CASE 2.—**A farmer was kicked by a horse. After suffering intensely for one week, he consented to have the fragments immobilized. Within three days he was consuming a regular diet, and in seven days he was

5. Waldron, C. W.: Skeletal Fixation in the Treatment of the Fractures of the Mandible, *J. Oral Surg.* 1:59-83 (Jan.) 1943.

6. Thoma, K. H.: Fractures and Fracture Dislocation of the Mandibular Condyle, *J. Oral Surg.* 3:3-59 (Jan.) 1945.

oing regular work on the farm. The pins were removed in the office at the end of eight weeks.

**CASE 3** (figs. 4 and 5).—The patient was a man, aged 8. A roentgenogram showed a transverse fracture of the right mandible at the junction of the horizontal and the ascending ramus which transversed the entire width of the bone, splitting the alveolus of the wisdom tooth. There was a dislocation inward of the proximal fragment. The third molar in the crevice was extracted and four pins inserted, two horizontally and two vertically.

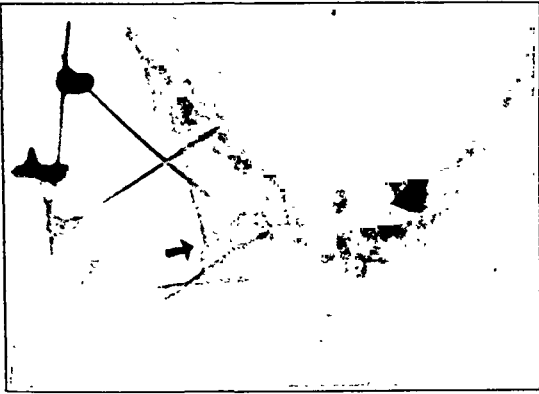


Fig. 4.—Perfect alinement of an angle fracture.



Fig. 5.—Placement of pins in an angle fracture.

cally. This patient, as well as the preceding patient, had an excellent resultant bite.

**CASE 4.**—A young woman, aged 28, was injured in an automobile accident. She had a shattering fracture of inferior mandible at the left mental foramen. She also suffered a crushing fracture of the left superior maxilla, with the left alveolar process pushed up to the left orbit. In addition, there were fractures of the right femur and both ankles. The patient was in a state of physical and mental prostration. Her mandible was fixed by skeletal fixation first. Her mental and physical condition cleared at once after the comfortable and permanent fixation of this painful fracture. Three days later the shattered fragments of the left superior

maxilla were molded. The loss of the upper left central incisor, lateral incisor, cuspid, first bicuspid, second bicuspid and first molar greatly weakened the area. The second and third molars were brought into alinement and held in position by a Straith mouth piece. A screw was placed in the left inferior orbital ridge, and this was held out by a bar from a Straith head splint buried in plaster. After these fractures were fixed the other fractures were corrected. The superior maxilla fractures were healed in six weeks; the inferior mandible was held firmly in place for eight weeks. Roentgenograms then showed the fracture firmly healed and so the pins were removed. Prosthetic restoration was satisfactory both from the esthetic and the functional standpoint.

**CASE 5** (figs. 6 and 7).—A girl, aged 18, was a passenger in a pleasure car which was in head-on collision. She suffered no injuries other than four fractures of



Fig. 6.—Four fractures of mandible, bilateral condylar, left angle, and symphysis crushed.



Fig. 7.—Close-up showing how pins were placed to hold all fragments. The plaster cap and supporting rod were used for ten days, as the masseter muscles were so bruised that the patient could not keep her mouth closed, and she complained of her throat becoming dry. In ten days this plaster cap was removed and all motions of the jaw were freely permitted.

the inferior mandible, the loss of the four lower incisors and the partial loss of her lower lip 0.5 inch (1.3 cm.) wide at the left angle of her mouth, tapering to an apex toward the right angle.

The fractures consisted of a shattering of the symphysis and a transverse fracture of the left angle at the junction of the horizontal and the ascending ramus which transversed the entire width of the bone. Both condyles were broken off  $\frac{5}{8}$  inch (1.6 cm.) below the condylar process. The proximal fragments were both pushed to the right and the distal fragments were overriding to the left. Two pins were placed in the small stumps of the condylar processes. After that it was fairly easy to manipulate and fix the fractures. We had a great deal of trouble visualizing these fractures with roentgen ray. This girl's bite is not perfect, but it is functional. The pins were removed in ten weeks.

#### CONCLUSIONS

These cases were not selected from the files of a large hospital clinic. The patients presented themselves over a short period in the medical

offices of a small community. They are cases which any physician or dentist may receive any day. Their importance lies in the fact that they illustrate the universal satisfaction which both physician and patient derive from this method of handling such difficult cases. The fractures can be reduced immediately; free movement is restored to the jaws; the whole process is clean and easily cared for, and the patient resumes normal activity in a minimum of time.

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#### CORRECTION

In the article by Kenneth W. Penhale, D.D.S., M.D. entitled "Acrylic Resin as an Implant for Correction of Facial Deformities," in the May issue (*ARCH. SURG.* 50:233, 1945) the reference in the first line of the legend for figure 8 should be to figure 7 instead of to figure 3.

## PROGRESS IN ORTHOPEDIC SURGERY FOR 1944

A REVIEW PREPARED BY AN EDITORIAL BOARD OF THE AMERICAN  
ACADEMY OF ORTHOPAEDIC SURGEONS

### VI. CONGENITAL DISLOCATION OF THE HIP

PREPARED BY A. BRUCE GILL, M.D., PHILADELPHIA

Turner<sup>170</sup> stresses the importance of early diagnosis and treatment of congenital dislocation of the hip. He feels that complications become worse with delay. The physical signs are listed as: I. Unilateral dislocation: (a) apparent shortening, (b) decrease in range of abduction, (c) piston motion, (d) asymmetry of skin folds about the thighs, (e) palpation of the head of the femur, (f) trochanter affected near the anterior superior spine. II. Bilateral dislocation: (a) wide perineum, (b) apparent lordosis, (c) unusually deep skin folds, (d) trochanters unusually near level of anterior superior spines, (e) palpation of femoral heads. It is noted in the roentgenograms that in congenital dislocation (1) the acetabular roof is sloping more than the normal 170 degrees, (2) the acetabulum is shallow, (3) the epiphysis is smaller, (4) the epiphysis is displaced, (5) Shenton's line is disturbed and (6) the metaphysial beak is displaced more laterally. The treatment should start as soon as possible. The complications are anteversion of the neck and aseptic necrosis.

Thompson<sup>171</sup> discusses primary acetabular dysplasia as the basic factor in congenital dislocation of the hip. The condition is hereditary and may be transmitted through either side of the family. This dysplasia may be recognized in the early weeks of life by the obliquity and the shallowness of the acetabulum as seen in roentgenograms of the hips. Dislocation may or may not occur, depending on the degree of the imperfection of the acetabulum, but if the dysplasia is not corrected during the period of growth the hip will always be abnormal, even though frank dislocation does not develop.

Natural growth processes will frequently overcome the dysplasia and cause a normal development of the acetabulum and of the head of the

femur if the normal mechanics of the hip are restored and maintained. Early treatments to take advantage of normal growth from the beginning are imperative.

The author reviews the clinical and roentgenographic evidence of "predislocations" of the hip. [Ed. NOTE.—I attach more importance to limitation of abduction than to asymmetry of the gluteal folds.] Predislocation should be treated by maintaining the hip in abduction and internal rotation until a roentgenogram shows that the hip has developed normally.

Dislocation should be reduced as soon as the diagnosis is made. Careful bloodless reduction is generally employed. If the dislocation cannot be reduced by manipulation or if reduction is not maintained, open reduction should be performed. Thompson has performed open reduction on a patient at as early an age as 5 months. He believes that the acetabulum develops more rapidly after open reduction than during fixation in a position of incomplete reduction. He advises osteotomy six weeks after open reduction, to correct anteversion of the neck. Fixation in plaster for six months after the open reduction is followed by unrestricted use of the extremity, without further orthopedic treatment. Periodic roentgenographic check-up is advocated thereafter until it is apparent that the hip joint has developed normally.

Lapin<sup>172</sup> discusses predislocation and describes 3 cases of suggestive physical signs of inequality of the two hip sockets, e. g., waddle gait, limp and asymmetry of buttock folds. In all the cases the roentgenologic examination shows normal conditions. A possible explanation offered is that on one side there may be a long capsular ligament or an intracapsular tissue of increased volume.

Michail<sup>173</sup> suggests that poor results in reduction are often due to difficulty of immobilizing

170. Turner, V. C.: Importance of Early Recognition of Congenital Dislocation of the Hip, M. J. Wisconsin 43:613-617 (June) 1944.

171. Thompson, F. R.: Early Diagnosis and Early Treatment of Congenital Dislocation (Acetabular Dysplasia) of the Hip, New York State J. Med. 44: 1095-1102 (May 15) 1944.

172. Lapin, H.: Pseudocongenital Dislocations of the Hip in Infants: Three Cases, Arch. Pediat. 60:649-652 (Dec.) 1943.

(Footnotes continued on next page)

the pelvis. He describes a pelvifixator, a steel plate with bars and straps devised by Nicod, which permits complete immobilization of the pelvis, with no interference with maneuvers, and causes no injury to the patient. Hitherto, to his knowledge no such apparatus has been described. A detailed illustrated description of the apparatus follows. Five cases are described in detail. Of 83 cases in which it was used, results were good in 23 and satisfactory in 29, and recurrences took place in 31. Results are much better in younger children than in older children. Non-surgical treatment is the method of choice, even for older children. If poor results are noted, surgical treatment should be instituted at about 5 years of age. For an irreducible congenital dislocation, osteotomy may be used.

Ponseti<sup>174</sup> made a study of 129 patients (one hundred and seventy-three hips treated) in the clinic of Dr. Arthur Steindler at the State University of Iowa College of Medicine to determine the factors which prevent normal development of the hip during the course of treatment for congenital dislocation of the hip. All patients were under observation for more than four years.

The author divides his cases into three groups: (1) cases of prenatal dislocations, present at birth; (2) cases of postnatal dislocations, presenting predislocation at birth and progressing to complete dislocation, and (3) doubtful cases, seen after infancy, presenting both a primary and a secondary acetabulum, with the time of dislocation unknown.

Treatment of the first type is usually unavailing. The structures of the hip are too far removed from the normal.

Predislocation, discovered in the early weeks or months of life, is treated by some method of abduction. Almost uniformly good results are obtained in these cases. The head of the femur is maintained securely in the acetabulum, and normal growth of the acetabular roof takes place during this early period.

Complete postnatal dislocation should be reduced by gentle manipulation. The hip is then fixed in plaster in a position of 90 degrees of flexion and 60 to 70 degrees of abduction (Waldenström position) for a period of three to four months. Then, with the patient under anesthesia, the legs are placed in the Lange position with internal rotation and retained in

plaster for another two months. The author then maintains abduction by a bar between the feet. The bar is attached to plates on the shoes. A pin is put into the plate to limit outward rotation at 75 degrees and to permit free inward rotation. Movement of the hips is permitted by this apparatus. The appliance is kept on for from two to six months, depending on the development of the acetabulum. Walking is then permitted for two hours daily for the next month, and the time is gradually increased.

If bloodless reduction cannot be accomplished, open reduction is advised.

The author believes that failure to secure a successful result is due to (1) epiphysitis of the head, (2) tendency of the head to become subluxated when the child begins to walk and (3) osteosclerosis of the acetabular roof.

Leveuf<sup>175</sup> has noted that in congenitally dislocated hips reduced by orthopedic methods one may often find a deformity of the upper end of the femur, especially at the level of the head. Of 600 cases studied roentgenologically for late results, only 25 per cent showed good anatomic and functional results. In more than half of the remaining 75 per cent there was a deformity of the head of the femur. Various theories of pathogenesis are reviewed. In reports of 12 biopsies of cartilage of the head removed at operative reduction, the histologic changes are described, including cavitation and ulceration. Nine specimens were from children of 2 to 5 years, and orthopedic treatment had been initiated at 8 or 10 to 14 months in 4 cases, at 22 months in 2 cases and at 30 months in 3 cases. All the patients showed pronounced lesions of the cartilage of the head of the femur, with changes similar to those seen in arthritis deformans. These observations show that orthopedic maneuvers for reduction may lead to severe and permanent lesions of the hip joint. Orthopedic reduction should always be attempted in cases of congenital dislocation of the hip, but under control of arthrography, which reveals any obstacles to reduction which would require surgical removal. This method avoids prolonged immobilization in a faulty position. In cases without cartilaginous lesions, the results were excellent. Perfect function can be hoped for in cases in which the joint has not been destroyed by futile orthopedic manipulation.

Nathanson and Lewitan<sup>176</sup> report 3 cases showing the association of spina bifida and dis-

173. Michail, J.: Treatment of Congenital Dislocations of the Hip in Children, *Praxis* 32:695-700 (Sept. 30) 1943.

174. Ponseti, I.: Causes of Failure in Treatment of Congenital Dislocation of the Hip (Improved Method, Including Use of Abduction Bar), *J. Bone & Joint Surg.* 26:775-792 (Oct.) 1944.

175. Leveuf, J.: Pathology of Grave Lesions of Head of Femur Following Unsuccessful Attempt at Orthopedic Reduction of Congenital Luxations of Hip, *Mém. Acad. de chir.* 68:400-403 (Nov. 11-18) 1942.

location of the hips. The authors believe that the dislocations are the result of the neural defect produced by the spina bifida. They point out that in severe forms it is accompanied with other anomalies: anencephaly, hydrocephalus, talipes equinus and others. The abnormality most commonly occurs in the lumbosacral region, and the neurologic signs manifest themselves in the lower limbs. Often one group of muscles show fair power, whereas antagonists may show complete paralysis. This was the condition in the 3 cases presented. Urinary incontinence and, less frequently, fecal incontinence are present. Two types of dislocation are distinguished: (1) the endogenous, in which there is a developmental arrest in the acetabular roof, and (2) the dynamic, in which abnormal forces are present, e. g., relaxation of the hip ligaments and imbalance of the muscle. The dislocation usually

occurs in the absence of power of the abductor and external rotator muscles. In the latter cases, maldevelopment of the acetabulum due to disuse follows.

Roberts<sup>177</sup> emphasizes the necessity of constructing the shelf or buttress above the head of the femur in such a manner that the new portion of the acetabulum is molded on top of the head and continues the arc of the circle which is present in the original acetabulum. [ED. NOTE.—It is often necessary to revise the arc of an oblique acetabulum by reflecting the roof downward.] He describes the method of open reduction and of closing the capsule with sutures so that the capsule overlaps the margin of the newly constructed shelf. He employs a bone strut to fix the iliac bone flap in firm contact with the head.

176. Nathanson, L., and Lewitan, A.: Spina Bifida Associated with Dislocation of the Hip, *Am. J. Roentgenol.* **51**:635-638 (May) 1944.

177. Roberts, F. B.: Plastic Shelf Operation for Dislocations of the Hip, *Ohio State M. J.* **40**:650-656 (July) 1944.

## VII. TUBERCULOSIS OF BONES AND JOINTS

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During 1944 there were comparatively few articles on the subject of tuberculosis of bones and joints of sufficient interest to include in a review of progress. However, it is encouraging to note an increase in experimental studies toward developing inhibiting or bacteriostatic agents that may be effective against tuberculosis. The effect of a number of sulfonamide compounds, including Diasone and promin, has been studied by a number of investigators, both in the laboratory and on human patients. The results appear to justify the hope that some important result may be expected, although the subject still is in the experimental stage.

In a study by Petter and Prenzlau,<sup>178</sup> Diasone (disodium formaldehyde sulfoxylate diamino-diphenyl sulfone) was therapeutically administered to 78 tuberculous patients for periods ranging from sixty to two hundred and seventy-five days. Seventy-two of the patients had pulmonary lesions, 5 had lesions of bones and joints and 1 had genitourinary lesions. The drug was given orally to all patients and applied locally as well to empyema cavities and abscesses about joints. The dose was usually 0.33 Gm. with meals (1 Gm. per day). Toleration was improved if the drug was started at 0.33 Gm. per

day for three days, increased to 0.66 Gm. for the next three to five days and then raised to the standard dose of 1 Gm. per day. Enteric-coated capsules gave less gastric disturbance. Evidences of toxicity were headache, gastric upset, palpitation, malaise, occasional visual disturbances and "blue skin." Also noted in some patients were an increase in temperature and an increase in cough and expectoration at the onset of treatment. None of these reactions were alarming in severity, none were unbearable and none irreversible. In 3.7 per cent of the cases, the drug was stopped because the patients preferred not to experience the unpleasantness of reactions. Studies of the blood showed an average initial drop from 4,700,000 red cells and 12.5 Gm. of hemoglobin to 2,700,000 red cells and 8.8 Gm. of hemoglobin in the third and fourth weeks and then a gradual rise to about 4,000,000 red cells and 10.3 to 11 Gm. of hemoglobin. Depression of the total leukocyte count did not occur, and neutropenia was not observed. Evidences of damage to the kidneys or liver were not observed clinically or by histologic study in 4 cases coming to autopsy after twelve to seventy-two days of full doses of the drug. With administration of 1 Gm. of Diasone daily, blood levels were maintained between 1.5 and 2 mg. per hundred cubic centimeters. In a small group of cases, the concentration of "free" Diasone in the blood ranged from 1.7 to 2.5 mg., in the cerebrospinal fluid

178. Petter, C. K., and Prenzlau, W. S.: Observation on Clinical Application of Diasone in Human Tuberculosis (Eight Month Study), *Illinois M. J.* **85**: 188-197 (April) 1944.

from 1.5 to 2 mg., in the urine from 44 to 80 mg. and in the bronchial secretion from 0.5 to 1 mg. per hundred cubic centimeters.

As the patients acquired a tolerance to the compound, general well-being improved and body weight remained at pretreatment level or increased. Cough and expectoration, in the presence of more acute lesions, increased at first and then gradually subsided. Conversion of sputum from positive for tubercle bacilli to negative occurred in 62 per cent of the patients treated from sixty to one hundred and twenty days. As observed by roentgen ray examination, clearing of parenchymal infiltration occurred in 75 per cent of patients, and there was also some increase in fibrosis. These changes for the most part began to take place at from thirty to sixty days. Closure of the cavity, or at least disappearance of cavity outlines, occurred in 37.5 per cent of 40 patients. In 34 patients, the blood sedimentation rate dropped from an average initial value of 45 mm. per hour (Westergren) to 10 mm. per hour after twenty-four weeks of therapy. Although most patients were bed patients and rest was probably a factor, similar favorable changes occurred also in patients who were ambulant and in others who continued to work full time. Four per cent of the patients, in whom the tuberculosis was far advanced, died after treatment for sixty days or longer; 6 per cent of the patients were considered worse, and in 3 per cent there was no apparent change. Improvement was recorded in 100 per cent of the patients with minimal disease, 90 per cent of those with moderately advanced disease and 76 per cent of those in far advanced stages. Improvement was recorded as slight in 22 per cent, moderate in 35 per cent and pronounced in 30 per cent. There were 5 patients with tuberculosis of bones and joints. One, with tuberculosis of a hip joint, was made worse, 2 were moderately improved and 2 were greatly improved. The authors conclude that Diasone, though not ideal, is an advance toward the goal of chemotherapy for tuberculosis and that it produced favorable changes in the majority of their patients in shorter time and of greater degree than would reasonably be expected on the regimen employed without the compound.

Feldman and Hinshaw<sup>179</sup> found that in experimentally induced tuberculosis in guinea pigs a daily dose of 200 to 250 mg. of Promizole had a therapeutic efficacy comparable to a daily dose

of 400 to 500 mg. of Promin (p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) and exerted a favorable influence even though treatment was not started until six weeks, ten weeks or fourteen weeks after animals had been inoculated with tubercle bacilli.

Feldman and Hinshaw<sup>180</sup> report experiments which indicate that 4,4'-diaminodiphenylsulfone is an effective agent in inhibiting or combating experimental tuberculosis in guinea pigs. Continuous prolonged administration yields cumulative benefits not attained in short term experiments. In the long term experiment, extending to two hundred and twenty-eight days, 71.4 per cent of the untreated animals died, while in the treated group only 28.6 per cent died. Histologic studies showed that the animals which had received the drug either were without demonstrable lesions or had residual foci in which the process was arrested, calcified or healed. Although producing some anemia, the drug was not excessively toxic for guinea pigs in the dose used. Efforts to modify 4,4'-diaminodiphenylsulfone to obtain a compound more suitable for clinical application should be encouraged, since the possibilities seem many.

Armstrong, Raie, Lucas and Greey<sup>181</sup> observed that Promin, used under the strictly defined experimental conditions of Feldman, Hinshaw and Moses, influenced favorably the course of experimental tuberculosis in guinea pigs. If, instead of the standard oral dose of 300 mg. per day for nine and ten months, 400 or 500 mg. per day was given for three to six weeks to animals which were perhaps more heavily infected, no therapeutic effect was noted.

According to Feldman, Hinshaw and Mann,<sup>182</sup> promizole (4,2'-diaminophenyl-5'-thiazolylsulfone) exerted a deterrent effect on previously established experimental tuberculosis in guinea pigs that was only slightly inferior to that of Promin. It produced moderate blood dyscrasia and goiter, but these effects were reversible. The low toxicity of Promizole for human beings and the tuberculochemotherapeutic properties of the drug in experimentally infected guinea pigs appear to justify its clinical trial.

180. Feldman, W. H.; Hinshaw, H. C., and Moses, H. E.: Effects on Experimental Tuberculosis of 4,4'-Diaminodiphenylsulfone, *Am. J. M. Sc.* **207**:290-305 (March) 1944.

181. Armstrong, A. R.; Raie, M. V.; Lucas, C. C., and Greey, P. H.: Effect of Promin on Experimental Tuberculosis, *Am. Rev. Tuberc.* **50**:160-162 (Aug.) 1944.

179. Feldman, W. H.; Hinshaw, H. C., and Mann, F. C.: Effects on Experimental Tuberculosis of 4,2'-Diaminophenyl-5'-Thiazolylsulfone (Promizole): Preliminary Report, *Proc. Staff Meet., Mayo Clin.* **19**:25-33 (Jan. 26) 1944.

182. Feldman, W. H.; Hinshaw, H. C., and Mann, F. C.: Promizole in Tuberculosis: Effect on Previously Established Tuberculosis of Guinea Pigs of 4,2'-Diaminophenyl-5'-Thiazolylsulfone (Promizole), *Am. Rev. Tuberc.* **50**:418-440 (Nov.) 1944.

Freedlander,<sup>183</sup> in a brief review, states that he has tested some ninety derivatives of benzophenone for their tuberculostatic effect in vitro. Benzophenone is low in toxicity and shows moderately high bacteriostatic action. The following derivatives increased the bacteriostatic action: 4-chloro; 2-chloro; 2,4' dichloro; 2-iodo; 4-methyl; 4-methoxy; 4-ethoxy, and thiobenzophenone. It was not possible to find a definite chemical pattern in the relationship between chemical structure and tuberculostatic action, but an optimal lipid-water solubility ratio was discernible.

Petter<sup>184</sup> published a note to bridge the gap between "news stories" and the appearance of proposed reports in medical literature. Diasone has been used in treatment of 139 patients. It is still an experimental therapeutic agent. Much more must be learned about dosage, toxic reaction, change which takes place in the tuberculous lesions and many other ramifications of such a problem. One cannot be too emphatic at this time in stating that this compound is not ready for even limited distribution until a great amount of investigational work is completed.

Buu-Hoi and Ratsimamanga<sup>185</sup> reported that dihydrochaulmugryl cinnamate in ethyl dihydrochaulmugrate administered to tuberculous guinea pigs resulted during the seventy-eight day period of the experiment in slower development of tuberculosis, a lowered mortality (30 per cent, as compared with 83 per cent in controls) and anatomically more discrete lesions as compared with those of control animals. In tuberculous guinea pigs on a diet low in ascorbic acid, the evolution of tuberculosis is more rapid than that in animals on a diet high in ascorbic acid.

Feldman and Moses<sup>186</sup> reported experiments in which diphtheria toxoid failed to exert any significant deterrent effect on tuberculosis experimentally induced in guinea pigs and rabbits.

Callomon and Groskin,<sup>187</sup> using promin, disodium formaldehyde sulfoxalate diaminodiphenylsulfone (compound 2398) and 4( $\alpha$ -pyridil-

N-sulfonamide) phenyl 2-azo-8-amino-1-naphthol 5,7-disulfonic acid (compound 2816), produced evident inhibition of the development of experimental tuberculosis in guinea pigs observed over a period of six weeks. Sulfanilamide, sulfapyridine, sulfathiazole and sulfathiazoline showed no appreciable effect under the same conditions of experimentation. Judged from mortality and histologic change, Promin produced the most beneficial results.

Penicillin, penatin and extracts of Raulin-Thom culture mediums of *Penicillium notatum* and *Penicillium cyclopium* were examined by Smith and Emmart<sup>188</sup> for their bacteriostatic action against tubercle bacillus in vitro, for their inhibiting action of tubercle formation on chorio-allantoic membrane of the chick embryo and for their chemotherapeutic effectiveness against experimental guinea pig tuberculosis. Extracts of the culture medium of *P. notatum* gave good but variable inhibition of growth of tubercle bacilli in glycerin bouillon. All the preparations tested appeared to have some activity in reducing the extent of tubercle formation on the chorio-allantoic membranes but did not decrease the incidence of infection. Penicillin exhibited no effect on experimental tuberculosis in the guinea pig; a slightly favorable effect was obtained with extracts of the culture mediums of *P. notatum*. At best, the chemotherapeutic activity of these preparations was slight compared with some of the sulfones previously investigated by the authors.

Schwartz<sup>189</sup> studied 4 rabbits given sub-arachnoid-suboccipital injections of tubercle bacilli. Meningitis, meningomyelitis, radiculitis, ganglionitis and tuberculoma developed. Following a review of the literature on experimental spinal tuberculosis, the author stresses the fact that in man the least frequent localization of tuberculoma is in the spinal cord. For the development of tuberculoma, not only the duration of the infection but probably the type and the dose of bacilli play a part. In most of the rabbits, paresis, paralysis and muscular atrophy developed. This is explained by the greater infiltration at the level of the cauda equina, which regulates motor sensibility and trophism of the hindlegs. This localization also favors limitation of the infection.

Hinshaw, Feldman and Pfuetze<sup>190</sup> studied evidence based on the administration of pro-

183. Freedlander, B. L.: Experiments in the Chemotherapy of Tuberculosis, California & West. Med. **61**: 85 (Aug.) 1944.

184. Petter, C. K.: Diasone in Tuberculosis, J. A. M. A. **124**:385 (Feb. 5) 1944.

185. Buu-Hoi and Ratsimamanga, A. R.: Ethyl Dehydrochaulmoograte Combined with Cinnamic Acid Derivatives in Experimental Tuberculosis, Compt. rend. Soc. de biol. **136**:772-774, 1942.

186. Feldman, W. H., and Moses, H. E.: Effect of Diphtheria Toxoid on Experimental Tuberculosis, Internat. J. Leprosy **11**:36-42 (Dec.) 1943.

187. Callomon, F. F. T., and Groskin, L.: Therapeutic Effect of Some New Derivatives of di-Amino-di-Phenylsulfone in Experimental Tuberculosis of Guinea Pigs, Tuberculoogy **7**:21-25 (Feb.) 1944.

188. Smith, M. I., and Emmart, E. W.: Action of *Penicillium* Extracts in Experimental Tuberculosis, Pub. Health Rep. **59**:417-423 (March 31) 1944.

189. Schwartz, L.: Experimental Tuberculosis, Dia méd. **16**:204-206 (March) 1944.

(Footnotes continued on next page)



mizole to 56 patients which indicated that this drug is unique among numerous compounds of this class studied in being easily administered, well absorbed and of extremely low toxicity for human beings. Evaluation of clinical results was not possible at this early period of the study.

Steenken, Heise and Wolinsky<sup>191</sup> state that Promin when fed by mouth exerts a definite retarding effect on experimental tuberculosis in guinea pigs and that vaccination with attenuated living tubercle bacilli combined with treatment with Promin induces a greater inhibition on the progress of the disease than treatment with Promin in the unvaccinated animals.

Auerbach and Stemmerman<sup>192</sup> present a study of 132 patients with pathologically proved tuberculosis of the spine, of whom 100 had roentgen ray examination within six months prior to death. The area involved was one vertebra in 6 cases (4 per cent), two vertebrae in 39 (30 per cent), three vertebrae in 24 (18 per cent) and multiple lesions in 63 (48 per cent). The area of spine involved was typically the dorsal portion, the lumbar portion, the sacrum and the lower and upper cervical portions, in that order. The disease develops in the vertebral body, and the intervertebral disk is involved by extrusion. Two types of pathologic lesion are described: 1. The productive type (sclerotic) shows bone of a yellow color which is firm and maintains its morphologic integrity; the disk remains intact, and the marrow spaces are filled with tuberculous granulation tissue which erodes but does not destroy trabeculae. 2. The exudative (caseous, destructive) type shows yellow bone with areas of liquefaction which may contain sequestrums; the bony architecture is completely destroyed by areas of caseation with extrusion to the disk, compression of the body and gibbus formation. Sixty-three per cent of destructive lesions were correctly diagnosed roentgenologically. Of 30 cases of productive lesions, none were diagnosed correctly.

After a comparison of postmortem roentgenograms with antemortem roentgenograms, it was felt that in some cases with a definite history of a primary focus diagnosis might be made by an

apparent sclerosis shown by roentgenogram. This sclerosis is thought to be caused by the productive changes seen in pathologic examination.

A case of a large cold abscess dissecting along the psoas, of ten months' duration, is discussed. The diagnosis of abscess was easily made. Roentgenograms consistently showed nothing abnormal, yet at autopsy nearly every vertebra was diseased, some partially but the majority completely.

When other roentgenologic evidence of vertebral tuberculosis is present, the possibility of the productive (sclerotic) type of disease should be considered. It is suggested that serial roentgenograms might be helpful in demonstrating changes in osseous density as the productive lesion progresses. Even when destructive lesions are typically present, the rest of the spine should be carefully scrutinized for evidence of possible productive disease. Evidence of "cold abscess" only is sufficient reason for careful roentgenologic studies of the spine for tuberculosis, although all other signs may be absent.

[ED. NOTE.—This study supplements an earlier one by Cleveland and Bosworth, in which the frequent occurrence of areas of necrotic sclerotic bone in tuberculosis of the spine was pointed out. These authors ascribed such lesions to ischemia caused by stripping of the periosteum by the abscess.]

Gill<sup>193</sup> presents the thesis that the pronounced shortening of the entire lower extremity sometimes seen in cases of tuberculosis of the hip is due not to disease but to premature closure of the epiphyseal cartilages of the femur or tibia or of both. He presents the histories of 15 cases of tuberculosis of the hip in which this complication occurred. In every case the onset of the disease was before the seventh year of age. The damage to the cartilaginous plate occurred not from any disease process but from pronounced decalcification of the bones and alteration in the cartilage, making it more susceptible to trauma. In 3 cases there was a diaphyseal fracture causing closure of the epiphyseal plates of both femur and tibia.

In order to prevent the occurrence of this complication, the avoidance of long periods of immobilization in plaster is advised whenever possible. It is suggested that the femur and the tibia be measured every six months in children with tuberculosis of the joints. If it is found that one of the epiphyseal cartilages has closed prematurely, an estimate of the final result in the

190. Hinshaw, H. C.; Feldman, W. H., and Pfuetze, K. H.: Clinical Administration of 4,2'-Diaminophenyl-5'-Thiazolesulfone (Promizole) in Tuberculosis: Preliminary Report, Proc. Staff Meet., Mayo Clin. 19: 33-36 (Jan. 26) 1944.

191. Steenken, W., Jr.; Heise, F. H., and Wolinsky, E.: Treatment of Experimental Tuberculosis in Vaccinated and Non-Vaccinated Guinea Pigs with Promin, Am. Rev. Tuberc. 48:453-460 (Dec.) 1943.

192. Auerbach, O., and Stemmerman, M. G.: Roentgen Interpretation of Pathology in Pott's Disease, Am. J. Roentgenol. 52:57-63 (July) 1944.

193. Gill, G. G.: The Cause of Discrepancy in Length of the Limbs Following Tuberculosis of the Hip in Children, J. Bone & Joint Surg. 26:272-281 (April) 1944.

length of the extremity should be made and an epiphysial arrest should be done in the opposite extremity at the appropriate time.

Mordasini<sup>194</sup> discusses the planogram as a valuable addition to the conventional roentgenograms in the diagnosis of tuberculosis in bone. A positive diagnosis can be made earlier. This technic is more useful in the frontal than in the lateral planes in tuberculosis of the spine. Case reports show that the early spinal lesion is not in the anterior part of the vertebra but that it starts in the central or the posterior portion of the body of the vertebra. Narrowing of the intervertebral spaces appears later.

[ED. NOTE.—The laminagraph has been proved to be of value in the detection of areas of tuberculosis of the vertebrae at the New York Orthopaedic Dispensary and Hospital.]

Meng and Wu<sup>195</sup> reviewed 70 cases of tuberculosis of flat bones of the vault, 40 of which had sufficient data for a definite diagnosis. Of the 40 cases, 20 were proved histologically and 5 by guinea pig inoculation or culture; 15 had sufficient clinical signs to justify the diagnosis. Eighty per cent of the patients were under 20 years of age. There were 23 men and 17 women. Trauma was not important or essential but may have been contributory. Eighty-five per cent had associated tuberculous lesions, and 50 per cent had pulmonary tuberculosis. Most lesions were, therefore, secondary hematogenous lesions starting in the diploe, and the tables were involved by extrusion. Two types of lesion are recognized: (a) the circumscribed (perforating) type of Volkmann (38 cases) and (b) the diffuse (infiltrating) type of Koenig (2 cases). There was a single lesion of the skull in 23 cases and multiple lesions in 17 cases. Most frequently involved were the frontal and the parietal bones because they contain a greater amount of cancellous bone. The onset was insidious, with only swelling evident. Pulsation of the mass indicates perforation of both tables. Differential diagnosis includes lipoma, sebaceous cyst, syphilis and

tumor. Results of roentgenologic examination are not typical and show only a round or oval single or a multiple punched-out defect. Aspiration is helpful. Treatment should be complete excision without drainage in the absence of a sinus, and the dura should be let alone. High voltage roentgen rays are sometimes of benefit.

Some of the causes of painful shoulder with radiation of the pain into the arm are discussed by Cohn.<sup>196</sup> No attempt is made to classify all the conditions which cause painful shoulder, but the diseases mentioned, with illustrative cases, are as follows: hypertrophic arthritis of the cervical portion of the spine, carcinoma metastasis to the cervical portion of the spine, herniated cervical intervertebral disk and tuberculosis of the cervical portion of the spine. The author also directs attention to these conditions which may be responsible for pain in the shoulder, i. e., cervical rib, the various neuritides and local lesions of the shoulder region, including arthritis, peri arthritis, bursitis and tears of the supraspinatus tendon. A careful and detailed physical and roentgenographic examination is stressed as a necessary means of securing an accurate diagnosis.

The author observes that referred pain in tuberculosis of bones and joints is a common symptom, and any complaint referable to the shoulder, especially in the absence of definite physical abnormalities, should make one suspicious of a lesion of the cervical portion of the spine. Roentgenographic studies of the cervical portion of the spine should always be made in cases in which pain in the shoulder is the symptom, especially when local signs are absent, because not infrequently advanced changes will be noted on the roentgenogram even when the patient does not complain of symptoms referable to the neck. The author believes that the *modus operandi* of the referred pain in many cases of tuberculosis of the cervical portion of the spine is due to compression of the nerve roots by tuberculous granulation tissue. The referred pain, as a rule, promptly responds to immobilization of the cervical portion of the spine in a plaster cast.

196. Cohn, B. N. E.: Painful Shoulder Due to Lesions of Cervical Spine, *Am. J. Surg.* 66:269-274 (Nov.) 1944.

194. Mordasini, E.: Beitrag zur Tomographie der Knochen und Gelenke unter besonderer Berücksichtigung der Knochen und Gelenktuberkulose, *Schweiz. med. Wchnschr.* 74:123 (Feb. 5) 1944.

195. Meng, C. M., and Wu, Y. K.: Tuberculosis of the Flat Bones of the Vault: Forty Cases, *Chinese M. J.* 61:155-171 (April-June) 1943.

#### VIII. CHRONIC ARTHRITIS

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The appearance of arthritis and rheumatic fever in the armed forces has spurred further investigation and the development of special

services for their treatment. The newer antibiotic substances have been carefully studied in attempts to prevent or relieve these diseases.

Most of the papers appearing during the year are concerned with some special symptom or special type of treatment. In a general paper, Wright<sup>197</sup> describes the importance of arthritis as a disabling disease. He states that it is ten times as common as tuberculosis or diabetes and seven times as common as cancer. In England chronic arthritis causes one sixth of the industrial disability and accounts for one tenth of the money for pensionable invalidity. He advocates the establishment of special clinics with trained personnel and proper facilities for physical therapy. He compares the problem to public health with that of tuberculosis.

A number of papers discuss possible etiologic factors. The problem of allergy in relation to sensitivity to food in the development of arthritis as it appeared in 10 personally observed cases is discussed by Turnbull.<sup>198</sup> In the patients the arthritic symptoms disappeared when the foods to which they were sensitive were eliminated. To determine the sensitivity, repeated tests are necessary. Selye and his co-workers<sup>199</sup> believe that the adrenal cortex can play an important role in the pathogenesis of rheumatic and rheumatoid conditions in man. In laboratory animals, administration of desoxycorticosterone acetate in large doses caused nephrosclerosis, Aschoff bodies in the heart and periarteritis nodosa. Arthritis was found in a few animals. Arthritis was found with much greater frequency if thyroidectomy had been performed on the animals or if the adrenal glands had been removed, especially if the animals had been kept in cold surroundings. In such instances, arthritis was found in fourteen days. This arthritis resembled that found in rheumatic fever. Gauss<sup>200</sup> calls attention to the frequently observed relationship between disturbances in the biliary system and rheumatoid arthritis. Correction of disturbances in the biliary system often leads to relief of the arthritis. The author considers two possibilities. The gallbladder may be a focus of infection, or biliary disturbances may lead to metabolic faults. Jaundice often relieves arthritis temporarily. The relationship is obscure.

[Ed. NOTE.—In the development of the so-called prodromas of arthritis, a great number

of things have been suspected. Probably any prolonged physiologic disturbance can be a precursor of symptoms of arthritis, but whether rheumatoid arthritis is initiated by an infection, as I understand the term, is still uncertain.]

Lyford and colleagues<sup>201</sup> have observed 3 cases of polyarticular arthritis as a complication of granuloma inguinale. In 1 patient, there were ulceration in many of the joints and necrosis of bone. In another, there was involvement of two vertebrae and a hip joint. The third patient had lesions in the bones of the hand and forearm, but there were no joints involved. All the patients had fever and persistent anemia, but there were no sequestrums and no pus. Donovan bodies were found in articular tissues. Ropes<sup>202</sup> states that atypical, asymmetric or monoarticular arthritis was frequently seen in the early stages of rheumatoid arthritis. For such patients, diagnosis was difficult. For patients presenting atypical symptoms, adequate treatment with prolonged rest in bed could hasten remission and might prevent progression. Hench and Fox and Gilbert<sup>203</sup> studied the articular complications seen in 266 patients with epidemic cerebrospinal (meningococcic) meningitis. Three types of arthritis were seen: (1) symmetric polyarthritis of short duration and not severe seen in the first few days of the disease; in such cases there might be periarticular and intra-articular hemorrhage; (2) an articular effusion of varying degree coming on after the fifth day; in this type, infection seemed to be present and articular damage might follow, and (3) arthropathies associated with serum sickness; there was a serous effusion into the joint, of short duration and with a favorable prognosis. Arthritis was observed in 10 patients: in 4 of 215 patients observed in the ten years before chemotherapy was used and in 6 of 51 patients observed in the two years since sulfonamide compounds were used. The lessened mortality, the authors believe, had permitted the greater appearance of complications. Hench and Rosenberg<sup>204</sup> describe a type of disease of joints which they call palindromic rheumatism. There are repeated attacks of articular inflammation, with no lasting

197. Wright, H. P.: The Challenge of Arthritis, *Canad. M. A. J.* **51**:264-265 (Sept.) 1944.

198. Turnbull, J. A.: Changes in Sensitivity to Allergic Foods in Arthritis, *Am. J. Digest. Dis.* **11**:182-190 (June) 1944.

199. Selye, H.; Sylvester, O.; Hall, C. E., and Leblond, C. P.: Hormonal Production of Arthritis, *J. A. M. A.* **124**:201-207 (Jan. 22) 1944.

200. Gauss, H.: Review of Role of the Biliary System in Arthritis, *Am. J. Digest. Dis.* **11**:271-276 (Sept.) 1944.

201. Lyford, J., III.; Scott, R. B., and Johnson, R. W., Jr.: Polyarticular Arthritis and Osteomyelitis Due to Granuloma Inguinale, *Am. J. Syph., Gonorr. & Ven. Dis.* **28**:588-610 (Sept.) 1944.

202. Ropes, M. W.: Rheumatoid Arthritis: Atypical Forms, *Bull. New England M. Center* **6**:54-56 (April) 1944.

203. Fox, M. J., and Gilbert, J.: Meningococcus Infections with Articular Complications, *Am. J. M. Sc.* **208**:63-69 (July) 1944.

204. Hench, P. S., and Rosenberg, E. F.: Palindromic Rheumatism, *Arch. Int. Med.* **73**:293-321 (April) 1944.

damage. Thirty-four cases are reported, 6 in detail. The patients had multiple inflammation, with subsidence of all symptoms between attacks. The cause was unknown. Usually the examination of the blood gave normal results, and the erythrocyte sedimentation rate was normal. Attacks provoked only transient slight elevations in the sedimentation rate. Pathologic examination of joints showed an increase in polymorphonuclear leukocytes in the synovial membrane. There might be a fibropurulent exudate. Between attacks, tissues of the joints revealed no significant evidence of inflammation. Treatment for the most part was symptomatic, usually heat and analgesics during attacks. Of 27 patients followed, 15 per cent were well, 44 per cent had improved and 26 per cent were in the same condition. Three patients were worse, and 1 had died. Not a single joint in these patients had been crippled.

[ED. NOTE.—The diagnosis of palindromic rheumatism should be made with great caution. Rheumatoid arthritis often develops slowly. I have recently seen 3 patients who had been studied in a large medical clinic and whose disease had been diagnosed as palindromic rheumatism. These patients later showed pronounced deformities and articular damage.]

Research projects have considered various phases of etiology, pathology and treatment of chronic arthritis. Waine and his associates<sup>205</sup> attempted to determine whether any toxic or infectious substance was excreted in the urine by patients suffering from rheumatoid arthritis. Urine from patients with active rheumatoid arthritis was passed through a filter, and 1 cc. was injected subcutaneously into the abdomens of 3 rats four times a week. Some of the urine was extracted with 70 per cent alcohol after absorption with kaolin. The extract was evaporated under a vacuum. The residuum was taken up in sterile isotonic solution of sodium chloride to make 5 cc. and adjusted to pH 7.4. One cubic centimeter was injected into each of 3 rats. Urine was also extracted with chloroform and evaporated under a vacuum. This was taken up in sesame oil and injected into 3 rats. The animals were killed in four months. No significant lesions were found. Rosenberg and co-workers<sup>206</sup> report the causes

of death of 30 patients suffering from rheumatoid arthritis. They found pulmonary disease the most common, causing death of 11 patients in this series. Cardiac disease was the cause for 9 patients; 7 of these patients had rheumatic heart disease. Renal disease was the cause of death of 3 patients, intestinal disease of 2, and miscellaneous causes of 5—cinchophen hepatitis, accidental death, carcinoma of the prostate, sudden unexplained death and cause unknown. The authors feel that there may be a relationship between unrecognized early rheumatic fever and the large number of deaths from cardiac disease. In only 10 of the patients was death in any way a result of the arthritis. Bayles and Riddell<sup>207</sup> studied the lipemia in three groups of patients with rheumatoid arthritis—10 patients receiving the usual nonspecific therapy, 11 receiving gold salt therapy and 4 whose arthritis was complicated by pregnancy. They found the total lipid, total cholesterol and phosphatide levels of the plasma and the lipid ratio normal in persons with active rheumatoid arthritis. Practically no change was noticed in the patients receiving gold salts. The lipemia of pregnant arthritic patients was similar to that of normal pregnant women. The amelioration observed on arthritis by pregnancy was not dependent on a correction of a lipid deficiency or on a shift in lipid ratios.

To determine the toxicity of gold salts, Freyberg and his associates<sup>208</sup> injected equivalent amounts of gold into rats, using compounds varying widely in their chemical and physical properties. They found that large doses of soluble gold salts (much larger than therapeutic doses) cause severe damage to renal tubules and glomeruli. The severity of the pathologic changes was in direct proportion to the amount of gold injected. No other organs showed important pathologic changes. Suspensions of gold in oil produced lesions in proportion to the solubility of the gold. Colloidal gold caused little renal damage, but reticuloendothelial cells packed with gold were observed in the liver and spleen after its injection. The dosage of gold could not be controlled by study of the plasma concentration of gold. In gold dermatitis, biopsies of the skin showed about the same amount of gold in the skin as was found in the skin of patients receiving gold who had no

205. Waine, H.; Bauer, W., and Bennett, G. A.: Effect of Subcutaneous Injection of Urine and Urinary Extracts from Patients with Rheumatoid Arthritis into Rats, *J. Lab. & Clin. Med.* 29:19-20 (Jan.) 1944.

206. Rosenberg, E. F.; Baggenstoss, A. H., and Hench, P. S.: Causes of Death in Thirty Cases of Rheumatoid Arthritis, *Ann. Int. Med.* 20:903-919 (June) 1944.

207. Bayles, T. B., and Riddell, C. B.: Plasma Lipids in Arthritis Patients Receiving Gold Salt Therapy and During Pregnancy, *Am. J. M. Sc.* 208:343-350 (Sept.) 1944.

208. Freyberg, R. H.; Block, W. D., and Preston, W. S.: Gold Toxicity in Relation to Gold Salt Therapy for Rheumatoid Arthritis, *J. A. M. A.* 124:800 (March) 1944.

dermatitis. Toxicity in most instances seemed to be an allergic reaction. The major factor in regard to toxicity was the speed of administration of the gold.

Turnbull<sup>209</sup> studied the toxicity and efficacy of massive doses of vitamin D in 30 patients with resistant chronic arthritis. The Steinbock process (ultraviolet-irradiated vitamin) vitamin D was used instead of electrically activated ergosterol (Whittier process). Toxic symptoms developed in susceptible patients and persisted as long as three weeks after the medication was stopped. In 80 per cent of the patients, toxic symptoms developed; 77 per cent were not improved in their arthritis. The author feels that electrically activated ergosterol is safer and more effective than other types of vitamin D given in large doses.

Davies<sup>210</sup> studied the synovial fluid in the joints of cattle between the ages of 1 and 4 years, just after they were slaughtered. He found the volume of individual joints roughly proportional to the size. Determinations of the viscosity of synovial fluid from hip and hock joints were made. The lowest value was 3.3 and the highest 575 centipoises. Values of over 150 centipoises were unusual. Forelimbs tended to have a higher viscosity than hindlimbs. Variations in viscosity were not due to variation in mucin content. The average total nitrogen content was 162 mg. per hundred cubic centimeters. Observations supported the view that synovial fluid is, at least in part, a dialysate from the blood with the addition of mucin, possibly from connective tissue.

In a study of the innervation of articular tissues Freyberg<sup>211</sup> found by staining with osmic acid three types of nerve endings: (1) free nerve endings, which may be on the surface of synovial cells; (2) an oval laminated end organ, usually deeper in the fibrous portion of the capsule, and (3) a fine network surrounding arterioles. No nerves were found in articular cartilage or in compact bone. All other articular structures were abundantly innervated. Pain fibers were distinct from those for touch and pressure. In patients there was a tremendous variation in the description of pain, although there was only a slight variation in the individual threshold for pain.

Sprague and McGinn<sup>212</sup> found that rheumatic fever and acute arthritis accounted for 0.38 per cent of the casualties and that rheumatic fever alone accounted for approximately 0.17 per cent, and combined with arthritis 0.33 per cent, of all causes for evacuation of men from the South Pacific area. Fatigue, exposure and infection of the upper respiratory tract were the activating mechanisms in bringing on an attack. They found that rheumatic fever existed among the natives of the tropics.

S. A. Goldberg<sup>213</sup> studied surgical and autopsy material to determine the earliest changes which appeared in chronic arthritis. The first changes in rheumatoid arthritis were in the synovial membrane and periarticular tissues, followed by changes in the articular cartilage and bone. The earliest changes were rarely seen in human beings but could be observed in laboratory animals. The characteristic changes in degenerative arthritis were in the articular cartilage. There was first a thickening and softening of the cartilage cells. This was followed by fraying and degeneration.

In a general paper Bach<sup>214</sup> discusses the medical treatment of rheumatic disease. In every case, social and economic factors played an important part in the development. Bach's plan of treatment consisted in four to six weeks of hospitalization in an attempt to arrest the disease and prevent crippling. Rest and relaxation were the first part of the treatment. Exercises in bed were given to induce relaxation, to improve thoracic capacity and to improve body mechanics. Casts were used to correct deformity. General irradiation and iontophoresis of the affected joints were carried out. Drugs, usually acetylsalicylic acid, were used to relieve pain and to correct any physiologic disturbance. Gold salts were given if the sedimentation rate was high; toxic manifestations were avoided. A diet which was adequate in protein and which was not too bulky was given, usually about 2,000 calories. As the patient improved, class exercises and remedial occupational therapy were given. Usually there was a long period of convalescence before the patient returned to work.

209. Turnbull, J. A.: Study of One Hundred and Twenty-Seven Cases of Arthritis, *Am. J. Digest. Dis.* 11:122-130 (April) 1944.

210. Davies, D. V.: Volume, Viscosity and Nitrogen Content of Synovial Fluid, *J. Anat.* 78:68-78 (April) 1944.

211. Freyberg, R. H.: Symposium on Analysis and Interpretation of Symptoms: Joint Pain, *Clinics* 2: 1586-1619 (April) 1944.

212. Sprague, H. B., and McGinn, S.: Rheumatic Fever and Acute Arthritis as Causes for Evacuation from South Pacific Area, *U. S. Nav. M. Bull.* 43:1-3 (July) 1944.

213. Goldberg, S. A.: Pathology of Osteoarthritis, *Am. J. Clin. Path.* 14:1-23 (Jan.) 1944.

214. Bach, F.: Management of Early Arthritis, *Practitioner* 152:20-25 (Jan.) 1944.

[ED. NOTE.—This is a well considered program for treatment in early rheumatic disease. Treatment cannot be standardized because of the multiplicity of possible causes and complicating factors, but a general outline such as this is helpful. Unfortunately, physicians now get patients late in their disease, when a long period of medical and surgical rehabilitation is required. It will probably require a long period of lay and professional education before this program can be applied effectively.]

In therapeutic attempts against chronic arthritis, the newer antibiotic substances have been used, with indifferent success. Boland and his collaborators<sup>215</sup> report on the use of penicillin in the treatment of active rheumatoid arthritis in an army hospital. In rheumatoid arthritis hemolytic streptococci have always been under suspicion. The blood usually contains antibodies against streptococci, usually agglutinins, in high titer. The skin is usually hypersensitive to extracts of hemolytic streptococci. Ten men were treated for whom the diagnosis of rheumatoid arthritis was definite and in whom the damage was not so severe that irreversible changes in the articular tissues had taken place. These patients were given 1,200,000 to 3,200,000 Oxford units daily. The penicillin was given every three hours for from fourteen to twenty days. There were no untoward reactions, and the changes observed were slight. In 8 patients there were no subjective or objective changes. One patient felt worse. In 1, slight subjective improvement was found. In 1, there was moderate subjective and objective improvement. Results of laboratory tests, including leukocyte count, sedimentation rate and cultures and smears for bacteria in the synovial fluid remained unchanged. The appetite improved in 6 of the 10 patients. The authors felt that penicillin was not of value in the treatment of rheumatoid arthritis.

Powell and Rice<sup>216</sup> used penicillin in treatment of rats which had arthritis caused by a pleuropneumonia-like organism. Treatment with penicillin was ineffective. Gold sodium thiomalate (Myocrysine) was effective in controlling the arthritis but was extremely toxic to the laboratory animals.

215. Boland, E. W.; Headley, N. E., and Hench, P. S.: Treatment of Rheumatoid Arthritis with Penicillin. *J. A. M. A.* **126**:820-823 (Nov. 25) 1944.

216. Powell, H. M., and Rice, R. M.: Ineffective Penicillin Chemotherapy of Arthritic Rats Infected with Pleuropneumonia-Like Organisms, *J. Lab. & Clin. Med.* **29**:372-374 (April) 1944.

Rawls<sup>217</sup> used small doses of gold thioglucose (Solgonal B oleosum), which contained 50 per cent gold, for 100 patients. Five milligrams was given twice a week for three weeks, 10 mg. twice a week for the next three weeks and then 25 mg. once a week. In 42 per cent of the patients toxic symptoms developed. Half of these occurred before 100 mg. of gold had been given. The patients quickly recovered from toxic symptoms in such small doses. The severity and duration of toxic symptoms depended on the dosage. There were no fatalities. In 53 per cent of the patients there was pronounced improvement, with almost complete remission of symptoms. Twenty-one per cent were definitely improved; 12 per cent were slightly improved.

Kennedy<sup>218</sup> used subcutaneous deposits of a sulfonamide compound in powder form in treatment of chronic infectious arthritis. He believes that in chronic rheumatoid arthritis the affected joints and lymph glands become metastatic septic foci. For these patients he uses a drachm (3.9 Gm.) or more of sulfanilamide powder subcutaneously in the affected limb. He states that improvement was observed in 3 chronic cases.

Neostigmine to relieve muscular spasm in rheumatoid arthritis was used by Trommer and Cohen<sup>219</sup> on 19 patients. One cubic centimeter of neostigmine methylsulfate (in a dilution of 1:2000) and 0.6 mg. of atropine sulfate were given every other day. In addition 7.5 to 45 mg. of neostigmine bromide with 0.6 to 1.2 cc. of tincture of belladonna were given daily. Thirteen patients showed decreased muscular spasm, and motions were carried out more readily. The effect following injection comes on in fifteen minutes and may last several days. [ED. NOTE.—The editor has observed the effect of neostigmine in similar dosage on a large number of patients during the past two years. Any beneficial effect observed was slight and transient. No lasting benefit was observed from its use.]

The chronically swollen, painful joint is one of the greatest problems in arthritis. Crowe<sup>220</sup>

217. Rawls, W. B., and others: Analysis of Results Obtained with Small Doses of Gold Salts in Treatment of Rheumatoid Arthritis, *Am. J. M. Sc.* **207**:528-533 (April) 1944.

218. Kennedy, R. T.: Chronic Infective Arthritis and an Experiment with Subcutaneous Deposits of Sulfonamide Powder, *M. J. Australia* **1**:150-152 (Feb. 19) 1944.

219. Trommer, P. R., and Cohen, A.: Neostigmine in the Treatment of Muscle Spasm in Arthritis and Associated Conditions, *J. A. M. A.* **124**:1237-1239 (April 29) 1944.

220. Crowe, H. W.: Treatment of Arthritis with Acid Potassium Phosphate, *Lancet* **1**:563-564 (April 29) 1944.

states that the articular fluid in chronic synovitis is alkaline, while it is acid in acute inflammation of the joint. To decrease swelling, a 1 per cent solution of acid potassium phosphate in isotonic solution of sodium chloride was injected into two hundred and eighty-four swollen joints. All the swellings were caused by rheumatoid arthritis except six, which were caused by traumatic synovitis. Twenty cubic centimeters was injected into the larger joints. Nine of fourteen joints with chronic swelling cleared up after one treatment. Lasting improvement was obtained in three fifths of the cases, and temporary relief was seen in all except 1, in which the condition became worse after the injection.

Mantha<sup>221</sup> combined gold sodium thiomalate with theobromine and sodium salicylate. Thirty-five patients had been treated. He gave 0.003 Gm. of myocrysine every ten to fourteen days and a capsule of 30 grains (2 Gm.) each of theobromine and sodium salicylate three times a day before meals. Good results were obtained by this combination.

Lawson<sup>222</sup> advocates large doses of salicylates for multiple rheumatoid arthritis (Still's disease). For 14 children, 85 to 293 mg. per kilogram were given. Plasma levels of 300 mg. per cubic centimeter were maintained. Six daily doses were given. Nausea, vomiting and acidosis developed in 1 child. Two children had tinnitus after therapy by intravenous injections. There was a slight prolongation of prothrombin time in all patients receiving salicylates. Four children with Still's disease showed remarkable improvement, which continued as long as the salicylate level remained high. One and one-half grains (0.09 Gm.) per pound (0.5 Kg.) was given daily, with one-third as much sodium bicarbonate. The dosage was increased if the plasma levels did not rise above 250 mg. per cubic centimeter. After clinical evidence of activity was absent for two weeks, the salicylates were stopped.

Recovery from multiple arthritis complicated by amyloidosis was reported by Trasoff and colleagues.<sup>223</sup> To a girl of 14, with low grade fever, palpable spleen and liver and a positive result of a congo red test, powdered whole liver was given for a number of months. The liver and spleen became no longer palpable, and laboratory findings became normal.

221. Mantha, L.: Combination of Sodium Gold Thiomalate and Theobromine with Sodium Salicylate, *Union méd. du Canada* **73**:271-272 (March) 1944.

222. Lawson, R. B.: Salicylate Therapy for Still's Disease, *North Carolina M. J.* **5**:477-482 (Oct.) 1944.

223. Trasoff, A.; Schneeborg, N., and Searf, M.: Recovery from Multiple Arthritis Complicated by Amyloidosis in Child, *Arch. Int. Med.* **74**:4-10 (July) 1944.

Douthwaite<sup>224</sup> advocates the use of bismuth in place of gold for certain patients. In 70 per cent of 200 patients treated with gold salts, symptoms and signs of arthritis disappeared, but relapses occurred in six months in the majority of the patients. Four courses of 0.8 Gm. each within two years seemed to eradicate the disease in 55 per cent. While gold is relatively effective, the great objection to its use is its toxicity. It probably acts by virtue of its being a heavy metal. Douthwaite began using bismuth, a less toxic heavy metal, in 1942. Twelve patients were given 0.2 Gm. of bismuth weekly, receiving 2 Gm. in ten injections. All these patients had clinically active disease and an elevated sedimentation rate. In 4, all evidence of the disease disappeared and the sedimentation rate became normal. In 2 good results were obtained: moderate improvement was observed in 4, and 4 showed no response to the bismuth. Most of these patients had a relapse in a few months. The authors felt that bismuth was beneficial but not so useful as gold. It was not of value for patients who failed to respond to gold. Its chief use was for those patients who could not tolerate treatment with gold.

Levinthal and his associates<sup>225</sup> discussed the organization of an arthritic clinic. For arthritis many varied therapeutic procedures are necessary. Every disability which the patient presents should be considered. Orthopedic management concerns itself with correcting anatomic derangement by the usual orthopedic procedures. Medical management concerns itself with upbuilding measures and with special therapy. The authors mention two: large doses of vitamin D; which is used when the disease has been present two or more years, and gold salts, which are used in the early cases.

Physical therapeutic measures in the treatment of arthritis are described by Snow.<sup>226</sup> In the treatment the physician must consider the psychologic status, the pain and disability, the prognosis and the patient as a whole. The types of physical therapy include moist heat, dry heat, massage, passive movement, rest, light, electrical modalities and exercise. The type and amount depend on the stage of arthritis. This therapy

224. Douthwaite, A. H.: Treatment of Rheumatoid Arthritis with Bismuth, *Brit. M. J.* **2**:276 (Aug. 26) 1944.

225. Levinthal, D. H.; Logan, C. E.; Kohn, K. H., and Fishbein, W. I.: Practical Management of Arthritis—Medical and Orthopedic, *Indust. Med.* **13**:377-379 (May) 1944.

226. Snow, W. B.: Relation of Physical Therapy to Arthritis, *New England J. Med.* **229**:959-965 (Dec. 23) 1943.

must be followed carefully and carried out by skilled technicians. It is of great help but of itself does not cure.

The role of surgical measures in the treatment of chronic arthritis is discussed by Colonna.<sup>227</sup> The orthopedic surgeon should be responsible for the prevention of deformity and the correction of whatever deformity has developed. In the hip, deformity develops in flexion and adduction, and osteotomy is sometimes required. In the knee the deformity is commonly flexion. An appreciation of the mechanical factors leading to deformity and the mechanical derangements induced by deformity is of prime importance in the rehabilitation of such patients.

A number of papers have considered the diagnosis, complications and treatment of gout.

Sézary and co-workers<sup>228</sup> state that gout is rarely localized to the extremities. They report on a patient in whom deposits of urates provoked inflammatory responses and required removal. [Ed. NOTE.—Faulty diagnosis for such deposits is common until pathologic examination reveals their true character.]

Bauer and Klemperer<sup>229</sup> discuss the medical management of gout. Hyperuricemia may result from decreased destruction, increased formation or decreased elimination of uric acid. In gout it is probably due to limitation of renal excretion of uric acid. Hyperuricemia is not the sole cause of deposition of urates in the tissues. The physiochemical factors which initiate the precipitation of urates are unknown. One cannot use determinations of serum uric acid levels as a measure of the efficiency of treatment, nor can they be used to predict an attack of gout. Colchicum is the drug of choice, but how it acts is unknown, since it does not decrease the hyperuricemia. In the treatment of acute gout, the preliminary use of a saline cathartic is recommended. Colchicine, 0.5 mg., should then be

given every hour until relief of symptoms or toxic symptoms appear—diarrhea, nausea and vomiting. Then one to two doses should be given daily. Fluid, 3,000 to 4,000 cc., and rest in bed should be given. Moist heat over the affected joint is helpful. The prevention of subsequent attacks is difficult; a low purine diet or a fat-free diet is ineffective, and a normal diet is not harmful. As far as can be determined, overindulgence in alcohol does not provoke an attack. Sézary and his colleagues advocate balanced diet, avoidance of foods with high purine content and avoidance of obesity. Colchicine, 0.5 mg. three times a day, with high fluid intake, a high carbohydrate diet and maintenance of an alkaline urine are recommended for long periods. Salicylates, however, are the safest drugs. Acetylsalicylic acid, 5 to 6 Gm. a day, may be used three days a week. This leads to the rapid excretion of uric acid. Attacks cannot be prevented by the continuous use of salicylates. Chronic gouty arthritis is least amenable to treatment. Here pain is due to permanent articular changes. Gout receives no special benefit from spa treatment. The cardiovascular and renal complications are not preventable and must be treated as they appear.

Bartels,<sup>230</sup> in an analysis of the cases of 14 patients with chronic gout, found during an eleven year period an average loss of twenty months from work, an average salary loss of \$3,640 and medical expenses of \$498. In order to prevent such losses, an interval treatment has been planned. This consists of a diet low in purine and fat and high in carbohydrate, with the periodic administration of cinchophen, 7½ grains (0.48 Gm.) three times a day for three days in the week. No alcohol is permitted. Since this diet is low in vitamins A and B, these vitamins are added. At times physical therapy is helpful. Thirty-one cases were studied in detail while the patients were on this regimen. Only seven minor attacks occurred, as compared with eighty-four major attacks during an equal period before treatment.

230. Bartels, E. C.: Successful Treatment of Gout, *J. Tennessee M. A.* **37**:5-9 (Jan.) 1944.

227. Colonna, P. C.: Role of Surgery in the Chronic Arthritic Patient, *Clinics* **2**:955-965 (Dec.) 1943.

228. Sézary, A.; Boulenger, P., and Malanjeau, P.: *Panaris*, *Presse méd.* **50**: 386-387 (June 10) 1942.

229. Bauer, W., and Klemperer, F.: Medical Progress in Gout, *New England J. Med.* **231**:681-685 (Nov. 16) 1944.

## IX. INFANTILE PARALYSIS

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*Etiology.*—Zahorsky's<sup>231</sup> chief purpose is to recall the experiments made by Dr. E. W.

231. Zahorsky, J.: Saunders' Theory on the Etiology of Poliomyelitis, *J. Missouri M. A.* **41**:162-164 (Aug.) 1944.

Saunders, who thirty years ago proposed his revolutionary hypothesis on the causation of acute anterior poliomyelitis. This hypothesis, as Dr. Saunders stated, was only a "working hypothesis," to be refuted or corroborated by



future clinical observations and laboratory experimentation. Briefly stated, Dr. Saunders' hypothesis was this: Poliomyelitis in its sporadic appearance has an aviary origin through the medium of the green fly (*Lucilia caesar*) as a host. In other words, poliomyelitis is conveyed by the ova or larvae of the green fly from a fowl or other animal which has died from a specific paralytic disease. Not only chickens but fowls of every species are affected by limberneck. The experiments of Dr. Saunders definitely proved that the larvae of the green fly or other species of blow flies developing on a fowl dead from limberneck produce symptoms of paralysis when ingested by other animals (young fowls or guinea pigs). The author states that the clinical experience in a large number of epidemics in the last thirty years has not refuted any of the clinical data collected by Dr. Saunders, and he wishes to call attention to Dr. Saunders' published articles, which contain many suggestive avenues of approach to experimental medicine.

**Transmission.**—Bortagaray<sup>232</sup> reports on the most recent poliomyelitis epidemic in Argentina. He states that there was an increased incidence of poliomyelitis observed in Argentina from 1942 to 1943 and also an increase in the more serious type of disease in adults and older children. He states that after use of the treatment prescribed by Sister Kenny there were fewer and less severe sequelae, deformities were fewer or less pronounced, the skin appeared more normal and the muscles and bones developed more normally. The immediate results of this treatment were excellent, with a high percentage of cures in the cases of the usually fatal bulbar type. General care included rest, doses of phenobarbital sodium every four hours, small doses of morphine and infusions of dextrose or isotonic solution of sodium chloride given intravenously. The respirator was needed less frequently, as there were fewer pure respiratory paralyses. Repeated spinal punctures relieved headaches and meningeal symptoms.

Walters<sup>233</sup> studied 100 cases of poliomyelitis from July 1 to Nov. 15, 1943 to determine the incidence of certain epidemiologic factors for this article. The report is as follows:

Twelve per cent of the patients had been swimming in water which may have been con-

taminated with sewage. This was not considered an important factor in the cases studied.

Use of water from shallow wells and use of no other sanitary facilities than privies were surveyed. Thirty-six per cent were regular users of well water, 11 per cent used cistern water and 2 per cent had used spring water; 54 per cent lived within 100 yards (90 meters) of one or more outdoor toilets.

In line with Aycock's conclusion that milk-borne epidemics of poliomyelitis are probably of the same frequency as epidemics of other infectious diseases which are occasionally transmitted through milk, 68 per cent had used raw milk for an indefinite time prior to their illness.

The high incidence in proximity of chickens to poliomyelitis victims noted in the study bears out Hammon's belief that the rural barnyard and the fowls of the semirural home are the chief sources of infection. Eighty-nine per cent of the patients surveyed had chickens on their own premises or within 100 yards of their homes. Sabin and Ward had concluded, after investigating the virus in insects, "We believe that the search for a reservoir of poliomyelitis virus among the lower animals is worth while and should continue. . . . We are inclined to regard poliomyelitis as a disease which occurs the year round but has a greater incidence during the summer and autumn because greater dissemination of the virus may be made possible by a number of factors, including insects such as flies." In Walter's study 12 per cent of patients lived within 100 yards of sheep or goats, 32 per cent owned or lived within 100 yards of horses, 38 per cent were within the same distance of hogs and 48 per cent within a similar distance of cows, 48 per cent owned cats, 59 per cent possessed dogs, 83 per cent acknowledged the presence of flies on their premises and 62 per cent had mosquitoes on their premises.

Ward and Melnick<sup>234</sup> state that the aim of their communication is not to make a plea for sewage or flies as vehicles in the transmission of the disease but to point out that contact infection has not been demonstrated to be the "most important means" of spreading poliomyelitis. It seems futile to insist on a "unitarian" theory of spread.

Virus has been kept in sewage at a temperature of 7 C. up to eighteen days. Low concentrations of residual chlorine destroy a fixed amount of Theiler's mouse poliomyelitis virus. This same amount of virus in the presence of extrane-

232. Bortagaray, M. H.: Most Recent Epidemic of Poliomyelitis in Argentina, *Rev. Soc. puericult. Buenos Aires* 9:413-418 (Oct.-Dec.) 1943.

233. Walters, O. S.: Possible Transmission Factors in Poliomyelitis, *J. Kansas M. Soc.* 45:163 (May) 1944.

234. Ward, R., and Melnick, J. L.: Spread of Infective Paralysis, *J. A. M. A.* 124:595-596 (Feb. 26) 1944.

us organic matter survives more than ten times this amount of residual chlorine.

Arguments against flies playing a role in transmission are as follows: 1. Flies are not invariably associated with the disease, as in winter poliomyelitis. 2. The disease would not attack children preponderantly, as is the case, if it were transmitted primarily by the fly or any other insect. One would expect just such a high incidence in children if adults were immune because of infection—preponderantly abortive or nonparalytic—acquired in childhood or immunity acquired by other, as yet unrecognized, means.

The probability of obtaining virus from flies trapped in epidemic areas would appear to be as good as that of obtaining it from stools and certainly better than that of finding it in nasopharyngeal washings.

Contact infection is admittedly a means of spread, but that it is "the most important means" has not been proved to the authors' satisfaction. Seasonal incidence cannot be explained in this way (epidemics fade out when school opens). The rarity of hospital infection from patient to patient and from patient to hospital personnel would militate against the philosophy of greater segregation as a solution, or even as an aid to a solution, to the problem.

The authors express the belief that it is wise to keep receptive minds to evidence which may eventually show other "modes of spread of infantile paralysis," more in keeping with present knowledge of the natural history of the disease.

Horstmann, Ward and Melnick<sup>235</sup> undertook a study to determine the average duration of excretion of virus in stools of patients following acute infection and to ascertain whether a chronic carrier state similar to that occurring in typhoid exists in poliomyelitis. The stools of 61 patients (46 paralytic and 15 nonparalytic) were collected during the first or second week of the disease and at four to six week intervals thereafter. The materials collected were frozen immediately or within a few hours after collection and stored on solid carbon dioxide until ready to be tested. The inoculum (prepared by Melnick's technic with a few minor changes) was ultracentrifuged at 39,000 revolutions per minute and inoculated into immature rhesus monkeys, by the intracerebral route in fifty-four tests, directly into the lumbar portion of the cord in eighty tests and by a combination of the two routes in twelve. All but 2 monkeys were ultimately killed, and the result of a test

considered positive when microscopic lesions characteristic of poliomyelitis were seen in the spinal cord. It was found that 61 per cent of the patients excreted virus during the first two weeks after onset of the disease, 50 per cent during the third and fourth weeks, 27 per cent during the fifth and sixth weeks and 12.5 per cent during the seventh and eighth weeks. Between the ninth and twenty-fourth weeks, virus was detected in only 1 of 52 specimens tested, 1 patient excreting it in the twelfth week. Not one of the 61 patients followed was demonstrated to become a persistent carrier of poliomyelitis virus.

Maxcy<sup>236</sup> states that present day conceptions of epidemiology of poliomyelitis rest in a large part on the observations made in Norway and Sweden toward the end of the nineteenth century and during the early part of this century, which are available in the classic monograph of Ivan Wickman, published in English translation in 1913. Studies in the United States began with the reports of Dr. Charles S. Caverley on the occurrence of anterior poliomyelitis in the state of Vermont in 1894 and were continued by Flexner and Lewis after the 1907 epidemic in New York and by W. H. Frost after the 1910 outbreak in Minnesota and Nebraska, the 1911 occurrence in Iowa, the outbreak in Cincinnati in 1911 and in Buffalo and Batavia, N. Y., in 1912. The largest epidemic which this country has experienced occurred in and about the city of New York in 1916 and was studied in great detail by three officers of the United States Public Health Service. C. H. Lavinder, A. W. Freeman and W. H. Frost. Since the publication of their report, the large number of contributions from investigators in this country and abroad have served to confirm, amplify and extend the basic observations, although the net advance has been relatively small.

After review of available morbidity and mortality data, with considerations of their limitations in mind, the following brief interpretations regarding broad general characteristics appear to be valid:

1. The disease is worldwide in distribution.
2. From no human community is the disease long absent.
3. Transmission can occur in any month of the year.

235. Horstmann, D. M.; Ward, R., and Melnick, J. L.: Persistence of Virus Excretion in the Stools of Poliomyelitis Patients, *J. A. M. A.* 126:1061-1062 (Dec. 23) 1944.

236. Maxcy, K. F.: A Review of the Epidemiology of Acute Anterior Poliomyelitis with Reference to the Mode of Transmission, *Journal-Lancet* 64:216-223 (July) 1944.

4. The disease exhibits an irregular interannual periodicity in prevalence.

5. From an original focus, the spread is progressive in unpredictable directions.

6. It has no regular pattern as regards rural and urban distribution if long periods are considered.

7. Poliomyelitis is characteristically a disease of early childhood.

8. Immunity to attack is acquired with advancing age.

9. The total number of patients manifesting characteristic paralysis during an epidemic period rarely exceeds 2 per thousand population of all ages.

10. The number of persons infected with the virus of poliomyelitis is far greater than is indicated by an attack rate based on reported cases of paralysis alone.

11. A considerable proportion of patients has had recent direct or indirect contact with a person who is known or suspected to have or to be convalescing from a paralytic or nonparalytic stage of the disease.

After illustrating the behavior of poliomyelitis in two local outbreaks (the first in Atlanta, Ga., in 1941 and the second in a small rural focus in the state of New York in 1940), the author states that the interpretation which seems most consistent with the facts and observations presented up to this point may be briefly summarized as stated by Lavinder, Freeman and Frost in 1916:

1. That poliomyelitis is, in nature, exclusively a human infection transmitted from person to person without the necessary intervention of a lower animal or insect host, the precise mechanism of transmission and avenues of infection being undetermined.

2. That the infection is far more prevalent than is apparent from the incidence of clinically recognized cases, since a large majority of persons infected become "carriers" without clinical manifestations (i. e., have had inapparent infections). It is probable that during an epidemic such as that in New York City a very considerable proportion of the population becomes infected, adults as well as children.

3. That the most important agencies in disseminating the infection are the recognized carriers and perhaps mild abortive cases ordinarily escaping recognition. It is fairly certain that the frank, paralytic cases are a relatively minor factor in the spread of infection.

4. That an epidemic of one to three recognized (i. e., paralytic) cases per thousand, or even less, immunizes the general population to such an extent that the epidemic declines spontaneously, due to the exhaustion or thinning out of infectible material. Apparently an epidemic incidence relatively small in comparison to that prevailing in an epidemic may produce a population immunity sufficient to definitely limit the incidence rate in a subsequent epidemic.

After examining the literature on the question of transmission, Maxcy says that it is uncertain whether the effective exit of the parasitic virus is via oropharyngeal secretions or by feces or by both. He analyzes the data available on transmission of fecal-borne pathogen by persons, flies and water, and he gives the technic used in establishing and then partially abandons the hypothesis of transmission by secretions of the oropharynx. His final conclusions are that it is within the realm of possibility that both mechanisms of transfer—the respiratory contact and the fecal contact—are operative and that each plays a role in maintaining passage of the virus through human populations.

Biermann and Piszczek<sup>237</sup> report on a case of poliomyelitis in a newborn infant in the epidemic of 1943 in Wichita, Kan. The mother had an uncomplicated pregnancy, with normal delivery. The onset of fever (temperature 100.6 F.) occurred eleven hours following delivery, with typical symptoms of acute poliomyelitis ensuing. There was complete paralysis of both upper and lower extremities, along with bulbar involvement. The patient became progressively worse and died on the fourth day post partum. The child (a normal boy) was seen by the mother for ten minutes four hours after delivery. The degree of contact was not observed. The child was normal until the eleventh day of life, when he became listless, febrile and cyanotic. The diagnosis of poliomyelitis was substantiated by laboratory observations, including study of the spinal fluid. Both upper and lower extremities and abdomen were involved at first, and later general improvement was noted but the right lower extremity continued paralyzed.

There were 164 persons who had the disease in the county in which this patient resided, 9 of these in the town district (the mother was the seventh and the child the eighth). The father and two other children were well throughout the mother's illness.

The authors state that the possibilities of infection in this case were: (1) fetal infection, (2) birth canal exposure, (3) contact exposure and (4) other contact exposures. In the absence of laboratory evidence that contacts of the child other than the mother were excreting poliomyelitis virus, it was, of course, impossible to determine the source of the infant's infection; however, it appeared to them that the available evi-

237. Biermann, A. H., and Piszczek, E. A.: A Case of Poliomyelitis in a Newborn Infant, *J. A. M. A.* 124:296-297 (Jan. 29) 1944.

dence suggested that infection occurred at time of birth or shortly thereafter.

Krumbiegel,<sup>238</sup> in discussing the transmission of virus diseases (specifically poliomyelitis) by water, states that pathogens causing communicable diseases known to be spread by water usually enter the body via the gastrointestinal tract and leave in feces or urine or both. Accumulated weight of evidence points toward the gastrointestinal tract as the probable portal of entry, and there are an increasing number of investigators leaning toward the belief that, although poliomyelitis is essentially a disease affecting the central nervous system, it may be a "digestive tract disease" in that the virus may enter the body through one end of the tract and leave by way of the opposite end. Virus is found repeatedly in stools during the second and third weeks of convalescence following paralytic or abortive attacks. Stools are known to have contained virus for as long as one hundred and twenty-three days. The virus is exceedingly stable, surviving a 50 per cent solution of glycerin for eight years, and it withstands low dilutions of phenol and 15 per cent ether. It is not surprising, therefore, that it may be demonstrable in sewage. The activated sludge method of treating sewage is effective in removal or destruction of the virus of poliomyelitis. The virus remains active for as long as one hundred and fourteen days in sterile water at room temperature in the dark. It also withstands freezing. Coagulation and sedimentation seem to produce a slight reduction in the total amount of virus in any suspension, proportional to the amount of virus present. Sand filtration has little if any effect. The addition of activated charcoal to the suspension is partly effective, and the addition of alum floc to the suspension greatly reduces the amount of virus. Chlorination studies are inconclusive, as they were not comparable to methods employed by water purification plants. To date, epidemiologic evidence fails to indicate that water is biologically of any importance as a medium of transmission. It would be necessary to show that the behavior of poliomyelitis in some places or at some times is dependent on contaminated water. This has never been done, and the known epidemiologic behavior of the disease is definitely not compatible with a theory of water-borne spread. Cold is not deleterious to the virus; hence, if water borne, poliomyelitis should occur commonly in winter months. Usually epidemics occur in scattered regions with no common water supply. If the disease

were water-borne, there should be an explosive onset with large numbers of cases, which is not the case. The prevalence of the disease has not been correlated with the degree of sanitary care surrounding different water supplies as determined by either bacteriologic examination or sanitary survey.

Casey and Hidden<sup>239</sup> give a most interesting account of George Colmer III (Kolmer; Sept. 21, 1807-Sept. 27, 1878), a physician who was born in London, England, but who resided at Springfield, Livingston Parish, La., from 1841 until his death, except for a short period when he had an office in New Orleans. His recently discovered "Diary C" covers the period from 1849 to 1878 ("Diaries A and B" have not been found) and records local and national events, clippings from medical and lay journals, pamphlets and advertisements, daily and careful observations on weather, flood stages, flowering of various plants, occurrence of various epidemics, local meetings and local news, such as births, deaths and marriages, observations on garden vegetables, fishing, prize-winning stocks and crops. Another volume, the daily journal of his medical practice from about 1842 to 1878, records brief abstracts of the history, physical examination and treatment of his patients, including two pages of periodic notes on his own physical condition. Dr. Colmer was civic minded and did much for his community, including the building and running of a slave hospital in which the daily board was \$1 and the medical fees in accordance with the malady. His greatest contribution, however, seems to be his observations on the epidemiology of poliomyelitis. Paralysis in children was noted in Philadelphia in 1792 during an epidemic of yellow fever, and 4 cases were noted by Badham in Workshop, England, in 1835. The pathologic changes of poliomyelitis were first described by Heine in 1840, but the first epidemic of the disease to be reported anywhere in the world occurred in 1841 in West Feliciana Parish, La., some 30 miles (48 Km.) from Springfield, La., and was published in *The American Journal of the Medical Sciences* by Dr. Colmer in 1843. His observations that the disease occurred in the form of an epidemic in a small rural area in late summer and fall, that it largely affected children of the teething age (1 to 2 years), that it was associated with paralysis and that most of the youngsters eventually recovered have not been much improved on during the past hundred years. His additional note that teething

238. Krumbiegel, E. R.: Transmission of Virus Diseases by Water, *Bull. Hyg.* 19:513 (July) 1944.

239. Casey, A. E., and Hidden, E. H.: George Colmer and the Epidemiology of Poliomyelitis, *South. M. J.* 37:471-477 (Sept.) 1944.

was probably a factor may also be apt, as the drooling saliva is probably infectious in the several days before the onset of the prodromal period. If "Diary B" could be found or the daily journal of his medical practice before 1842, the epidemic would probably have also been described in them in greater detail, as Dr. Colmer was an efficient reporter of other local events.

*Diagnosis.*—Pounders<sup>240</sup> gives a comprehensive report on the diagnosis and medical management of poliomyelitis. The onset usually occurs with mild general symptoms accompanied with disturbances of the upper respiratory and digestive tracts lasting twenty-four to forty-eight hours. Two to four days later fever recurs, along with signs of meningeal irritation, and in one to four days later motor disturbances appear. The disease may be arrested in any stage, and in most cases it does stop short of motor involvement. Later, blood serum contains antibodies against the virus. The temperature is usually about 102 F. for four or five days. There is headache (any type), vomiting, constipation or diarrhea, urinary retention (especially the first five days or so), dizziness, irritability, pains in the back and legs and general hyperesthesia. Coarse tremor, especially of the hands, is an important diagnostic sign. The patient looks sicker than the temperature would indicate, the face is flushed and has an anxious expression and the pulse is increased out of proportion to the fever. There is inability to flex the back. Deep reflexes are exaggerated and unequal. There may be meningeal signs. The spinal fluid count reveals some increase in pressure; it may be clear or slightly hazy. The cell count averages 100 to 200 but may be 10 to 1,400. It becomes normal after ten to fourteen days. Albumin and globulin are moderately increased, and sugar is normal or slightly increased.

Muscle dysfunction appears in two to five days, usually with maximum involvement within one or two days. The temperature usually returns to normal four to six days later. The virus is active as long as the patient is febrile.

The lower extremities are usually involved, with spasm of the hamstring muscles. Later there are weakness of the quadriceps and spasm of gastrocnemius muscles, with weakness of the anterior tibial group. In the upper extremities the deltoid and shoulder girdle muscles are most commonly affected. The anterior flexors of the neck are often weak.

Respiratory difficulty may be due to (1) involvement of the thoracic portion of the cord, with dysfunction of the intercostal muscles; (2) lesions of the cervical part of the cord, in the third and fourth segments, with involvement of the diaphragm, (3) bulbar lesions involving nuclei of the vagus nerve, (4) acute ascending so-called Landry's-type of paralysis showing successive intercostal, phrenic and bulbar involvement and (5) occasional pharyngeal paralysis resulting in pronounced respiratory difficulty because of excessive fatigue from the continual interference with respiration by unswallowed material in the pharynx or by actual aspiration of this material. The cranial nerve most commonly affected is the facial, and when it is the only one involved the patient is usually not very sick. In more than half the cases, the disease clears up entirely. Involvement of the third, fourth and sixth cranial nerves affecting the eye muscles is occasionally encountered.

In treatment, complete rest in bed is indicated. Sedatives to induce sleep should be used cautiously when there is evidence of respiratory or bulbar paralysis. Pain and tenderness and muscle spasm are best relieved by hot applications. The usual procedures recommended in care of a sick child are applicable—fluids, a high caloric diet of soft food and attention to elimination. The respirator should be used when indicated, but when the respiratory center is paralyzed the apparatus gives only temporary help and may even be harmful.

Murphy,<sup>241</sup> in making a plea for early diagnosis, states that this is imperative for best treatment. Diagnosis is largely clinical. Approximately 80 per cent of all cases in an epidemic area are so-called abortive cases. Symptoms are mainly those of an acute infection. A high titer of immune substance on virus neutralization tests is demonstrable later. During the acute febrile course of the subclinical or clinical case and the asymptomatic period of the clinical case, there are no immediate symptoms, physical findings or spinal fluid changes that are diagnostic. During summer and fall, alertness to symptoms of acute infection is necessary. Temperature ranges from 101 to 105 F., and there are headache and vomiting at the onset, constipation or loose stools, malaise and even drowsiness. Pain is inconstant (in the back, chest and abdomen); it may be due to hyperesthesia and may be sufficiently intense at times

240. Pounders, C. M.: The Diagnosis and Medical Management of Poliomyelitis, *J. Oklahoma M. A.* 37: 487-489 (Nov.) 1944.

241. Murphy, J. H.: A Plea for the Early Diagnosis of Poliomyelitis, *J. Omaha Mid-West Clin. Soc.* 5: 85-87 (Aug.) 1944.

o simulate other disease. The critical findings of differential diagnostic value depend on signs of cord, brain and nerve irritation and must be supported by physical findings. These are sometimes so extremely variable and changeable that they may be detected only by careful, deliberate and repeated examinations. The most important sign is nuchal rigidity, which is accompanied with or followed by spinal tenderness. Kernig's sign may appear early or not. Deep reflexes are present but variable (hyperactive to sluggish). The muscle groups or muscles presenting tremors are likely to be involved. Rigidity of muscles, deep tenderness, discrete areas of perspiration, irritation of rectal or vesical centers in the lumbar part of the cord, with resulting constipation or urine retention, all may be demonstrated. Bulbar involvement may have a rapid onset, with difficulty in swallowing, impairment of phonation, salivation and excessive mucous secretion, disorientation, delirium and coma.

Puncture of the lumbar part of the cord is of therapeutic value in reducing intracranial pressure. The spinal fluid is normal throughout the first febrile and asymptomatic stages of the disease. At the onset of the paralytic phase, the spinal fluid is clear, there is increased pressure, the cells may vary from 10 to 200, the total protein is increased and the fluid is sterile on bacteriologic examination and does not contain the virus. Hence, examination of the spinal fluid is important if the results are positive but not necessarily contradictory when values are normal. The blood count and sedimentation rate are not contributory to diagnosis. Differential diagnosis is important in acute poliomyelitis to rule out purulent meningitis, encephalitis, St. Louis encephalitis and occasionally acute arthritis. The cardinal points of early diagnosis are: (1) awareness of poliomyelitis, (2) history of febrile attack a few days previously, (3) headache and fever, (4) nuchal rigidity and spinal tenderness, (5) spasm, tremor or weakness in a muscle or muscle groups, (6) hyperesthesia or pain, (7) reflex changes and (8) cerebrospinal fluid changes if positive. The author states that (9) the serious grade of the disease is indicated by progressive course and that (10) it is impossible to diagnose subclinical cases in the acute stage.

*Prevention.*—Lumsden,<sup>242</sup> in writing on the epidemiology of poliomyelitis and measures for its prevention, states that the possibility of sev-

eral specific viruses of poliomyelitis is given weight by the fact that strains of the virus obtained in different outbreaks present pronounced differences biologically, serologically, immunologically and otherwise. There are many possible modes of transmission, but none are conclusive. Preventive measures suggested are: (1) cleanliness and maintenance of cleanliness (hygiene and sanitation); (2) systematic, intense and continuous fights on rats, mice, flies, mosquitoes, roaches, fleas, bedbugs, ants, insects and vermin; (3) strict sanitation regarding disposal of garbage, manure and excreta of poultry and birds; (4) screening of living and sleeping quarters; (5) purified water supplies and sanitary sewage systems with final disposal; (6) rigid sanitary and hygienic supervision of public eating and drinking places; (7) educational campaign to discourage potential droplet infection (coughing, sneezing, spitting, blowing and wiping); (8) reasonable discouraging of public assemblages by children under 6 years, and (9) restraining of young children from undue physical stress. Closing of schools, churches and theaters, as is often demanded by misled public opinion, is unjustified; placarding of the affected homes is advisable; proper isolation of patients is advisable to guard against superimposed infections. There should be rigid disinfection of discharges from nose and mouth and feces. Quarantine is not justified except for food handlers and persons in close contact with large numbers of children.

*Pathology.*—Dublin, Bede and Brown<sup>243</sup> report their findings on studies of muscles taken for biopsy from 3 patients with poliomyelitis and stained by the Ranvier method. They observed a degeneration of nerve fibers, motor end plates and muscle fibers in a degree commensurate with the degree of paralysis; an irregularity of distribution in keeping with an irregularity of distribution of injury to nerve cells of the gray matter of the spinal cord; a degeneration of nerve fibers, consisting largely in failure of axons to stain together with preservation of cellular elements of capsules of motor endings and of sheaths of Schwann; atrophy of muscle fibers appearing as pyknosis, beginning with loss of cross striations and increase of longitudinal markings; degeneration of muscle and nerve ranking probably secondary to injury to nerve cells of the spinal cord, and no definite evidence of activity of degeneration or regeneration.

<sup>242</sup> Lumsden, L. L.: Poliomyelitis: Its Epidemiology and Measures for Its Prevention, Texas Rep. Biol. & Med. 1:233-241, 1943.

<sup>243</sup> Dublin, W. B.; Bede, B. A., and Brown, B. A.: Pathologic Findings in Nerve and Muscle in Poliomyelitis, Am. J. Clin. Path. 14:266-272 (May) 1944.

Baker<sup>244</sup> states that in view of the numerous and comprehensive studies on the pathologic changes of poliomyelitis by many competent pathologists one cannot hope to offer any new or startling observations on this subject. However, because of the many conflicting viewpoints regarding the significance of the various pathologic changes, it would seem of definite value to review again the histopathology in an attempt to arrive at some acceptable conclusions concerning these lesions and their significance. These conclusions are as follows: 1. A review of the literature reveals an unusual consistency in the nature of the lesions described as occurring in poliomyelitis. 2. Six illustrative cases of poliomyelitis and polioencephalitis are reviewed and discussed. 3. From these cases, the following conclusions can be made concerning the pathologic changes of this disease: (a) Meningitis of a mild degree is one of the earliest lesions and occurs independently of any other changes. (b) Mesodermal-glial (interstitial) changes comprise one of the most striking features. These changes may also occur independently of any other changes, as indicated by their appearance among both structurally and functionally intact neurons as well as by their occurrence in regions where nerve cells are normally absent. (c) The neuronal involvement constitutes the most important alteration because of the associated functional impairment. The damage to many of the nerve cells is reversible, with many neurons regaining normal function. Other neurons, however, are irreversibly damaged.

*Complications and Sequels.*—Cooperstock<sup>245</sup> records 4 cases of atelectasis complicating acute poliomyelitis with involvement of respiratory muscles, in 3 of which unexpected recovery took place. He believes that pulmonary infections develop secondarily to atelectasis produced by obstruction of the bronchi by unexpelled exudate. In patients with poliomyelitis with involvement of respiratory muscles, there is diminished vital capacity due not only to poor tonus of these muscles but also to poor general condition and consequently poor tonus of all muscles. There is also impaired efficiency of the cough mechanism, which permits accumulation of mucus in the bronchi and even occlusion with resulting atelectasis. Stagnant mucus is also a good medium for growing organisms natural to this region, with secondary pneumonia as a result. The prophylaxis in such

cases is the avoidance of exposure to infections of the upper respiratory tract and the institution of treatment early when they occur. Use of a respirator is essential. The respiratory tract must be kept open by suction or bronchoscopy. The indication for removing such patients from respirators is not the ability to breathe freely and without effort but the ability to cough, which is the prime indication.

Wyllie<sup>246</sup> discusses a study concerned with a familial outbreak of poliomyelitis, which began with the introduction of facial palsy into a rural family, previously uninfected, by a single member of the family, which resulted in paralytic and abortive types of the disease in the other members.

Cranial nerve nuclei are regarded as the analogs of the anterior horn cells; hence they may be attacked by the virus of poliomyelitis. The facial nerve (seventh) is the cranial nerve most often involved. The type of facial paralysis depends on the site of the lesion.

(a) A supranuclear lesion produces unilateral facial paralysis, but the forehead can still be wrinkled (bilateral innervation).

(b) A nuclear lesion, such as occurs in poliomyelitis, results in unilateral paralysis very similar to Bell's palsy.

(c) A lesion between the pons and the geniculate ganglion produces flaccid unilateral paralysis of the face, usually associated with deafness due to the close proximity of the auditory nerve.

(d) If the lesion occurs in the facial canal below the geniculate ganglion, Bell's palsy is apt to be produced. A sensory disturbance often appearing early and transient is fairly common in poliomyelitis.

In the family outbreak a daughter visiting in the city returned home afflicted with paralysis of the right side of the face. Sixteen days later a sister had symptoms of meningitis with paralysis of the right side of the face. Thirty-six days after the sister returned home from the city a brother became acutely ill with paralysis of the abdomen and legs, and a diagnosis of poliomyelitis was made. The mother and another son suffered sharp attacks of "influenza," as they regarded it, but their symptoms were also suggestive of abortive poliomyelitis. The illnesses occurred in the period from August through October, at which time "refrigeration" of the "superficial part" of the facial nerve was unlikely. Since chills are doubtful causes of facial paralysis and a coincidental occurrence of

244. Baker, A. B.: The Central Nervous System in Poliomyelitis and Polioencephalitis, *Journal-Lancet* 64:224-233 (July) 1944.

245. Cooperstock, M.: Atelectasis Complicating Acute Poliomyelitis with Involvement of Respiratory Muscles, *Am. J. Dis. Child.* 67:457-462 (June) 1944.

246. Wyllie, J.: Facial Paralysis in Relation to Poliomyelitis: A Study of a Family Outbreak, *Canad. J. Pub. Health* 35:71-79 (Feb.) 1944.

2 cases of Bell's palsy followed by a case of paralytic poliomyelitis in the same family is highly improbable, it is suggested that the virus of poliomyelitis may have involved the nucleus of the seventh cranial nerve, just as it is known to attack the anterior horn cells of the spinal cord. Four years after the onset of the disease, both sisters exhibited a slight residual paralysis of the face and the brother a persisting flaccid paralysis of the right leg.

That additional information might be gained on the relation of tonsillectomy to poliomyelitis the records of the Manhattan Eye, Ear and Throat Hospital were consulted, and many thousands of patients for whom tonsillectomy had been performed were communicated with by mail. Page<sup>247</sup> reports on these data along with the records secured from the New York Department of Health, which showed a conspicuous increase in the number of poliomyelitis cases every other year as follows: 243 cases in 1937, 43 cases in 1938, 184 cases in 1939, 67 cases in 1940 and 404 cases in 1941. Of the 27,849 questionnaires sent out from the hospital, 8,915 were answered, and 1 instance of poliomyelitis was reported. Seven patients reported illnesses following tonsillectomy and adenoidectomy, and all of these mentioned some spinal involvement; 6 reported spinal meningitis (three months to four years after operation) and 1 a "spinal condition which causes nervousness" in a child aged 6.

Howe, Wenner, Bodian and Maxcy<sup>248</sup> report on the different technic used for demonstrating virus in the human nose and throat, which was employed at the New Haven Hospital in the summer of 1943. The attempt to vary the method employed in the past was made, since the attempts of the earlier years have been virtually abandoned in the face of readily isolated intestinal virus. Cotton swabs rubbed against the posterior wall of the oropharynx and the peritonsillar area were dropped into a fluid-tight container with 1 cc. of sterile water, stored on solid carbon dioxide and then eluted in phosphate buffer at  $p_H$  8, the fluid being pressed out of the cotton in a syringe. The eluate was then brought to  $p_H$  6 and treated with 20 per cent ether in the refrigerator until sterile (usually thirty-six hours), at which time the ether was removed. The entire inoculum obtained (in no case more than 1.1 cc.) was given to

rhesus monkeys of 8 to 10 pounds (3.6 to 4.5 Kg.) under ether anesthesia through a trephine hole made over the sagittal suture just posterior to the coronal sutures. An average of two swabs were obtained from 10 patients (paralytic or nonparalytic) during the first week of the acute illness. Fourteen specimens were used from the twenty collected, and seven (50 per cent) produced typical poliomyelitis in the test rhesus monkeys. Microscopic sections showed characteristic lesions in each case.

*Surgical Treatment.*—Debrunner<sup>249</sup> discusses a case of poliomyelitis in which not only organs and tissues were adapted to changed function but function itself was adjusted to changes in structure. A 4 year old girl with residual paralysis in the left leg, slight Trendelenburg position, pes cavus and pronounced paralysis in the heads of both biceps muscles and in the gluteal muscles was observed. In the foot there was a total paralysis of the anterior tibial and pronounced weakening of both other supinators. Her gait was impaired by faulty position of the foot, bearing weight only on the inner margin. She had received no planned treatment. To raise the foot, a small support was made from a plaster cast, which permitted walking in good position. After a year the support had to be altered slightly. A year later, when the mother came for repair of the support, it was noted that the impression of the sole had been changed to that of a normal foot. It is of special interest that a muscle of only secondary importance for the posture mechanism of the foot was brought into use for gait automatism. It is suggested that deformity might be prevented by training motor function.

Wiesenfeld<sup>250</sup> reviews the results of 17 cases of posterior bone block operations: 52.9 per cent were done by Briggs's modification of the Campbell bone block and 35.2 per cent were done by Gill's procedure. All the patients had had previous foot stabilizations. Of the series, 11.9 per cent had a combination foot stabilization, tendo achillis lengthening and posterior bone block. The results were considered excellent in 88.2 per cent of the patients operated on. There were two failures: in the first patient a painful arthritis of the ankle joint developed,

247. Page, J. R.: Tonsillectomy and Poliomyelitis. *Arch. Otolaryng.* 39:323-324 (April) 1944.

248. Howe, H. A.; Wenner, H. A.; Bodian, D., and Maxcy, K. F.: Poliomyelitis Virus in the Human Oropharynx. *Proc. Soc. Exper. Biol. & Med.* 56:171-172 (June) 1944.

249. Debrunner, H.: A Case of Physiologic Functional Adaptation of Plantar Muscles in Residual Paralysis. *Schweiz. med. Wchnschr.* 73:965 (Aug. 7) 1943.

250. Wiesenfeld, P. C.: Report of Seventeen Cases of Posterior Bone Block for Drop-Foot Seen and Treated at the New Jersey Orthopaedic Hospital, Orange, N. J., from 1933 to 1943. *J. M. Soc. New Jersey* 41:344-346 (Sept.) 1944.



and the second patient was a young woman who wished to wear high heels, although the foot was blocked at a 90 degree angle. This was later revised to give her 10 degrees of flexion.

[ED. NOTE.—I believe that in all cases of posterior bone block there should have been previously a stabilization by a triple arthrodesis. It appears to me that the triple arthrodesis, heel cord lengthening and posterior bone block is too much operative procedure to attempt to control at one sitting.]

Kleinberg<sup>251</sup> states that since there is no cure for scoliosis the treatment is consequently limited to two objectives: first, prevention of increase in deformity and, second, improvement or reduction of the curvature. Scoliosis complicating acute poliomyelitis is a more serious problem than the idiopathic and the nonparalytic curvature. The salient features that influence therapy are the following:

The plastic state of the tissue. The vertebrae become susceptible to structural alterations.

Onset. The onset is insidious.

Static imbalance. Unequal involvement of muscles of trunk and of pelvifemoral groups.

Progress of paralytic scoliosis. This may occur slowly or progress rapidly after a period of several years. It may increase after a seemingly adequate vertebral fusion.

Trophic changes. These occur in bones and are due to disturbed innervation and poor circulation.

Unknown etiologic factor. The etiologic factor is unknown.

Incidence. The incidence was 10 per cent in the author's cases and 30 per cent in the cases of Colonna and Von Saal.

Sex distribution. Cases were about equally distributed between the sexes.

Time of onset of paralytic scoliosis. In 50 per cent of cases the onset occurred in the first five years after the illness.

Muscle paralysis. About 75 per cent of the patients had involvement of abdominal muscles, with convexity of curve on weakened side.

Types and degrees of curvature. Two thirds of 34 patients had a single long curve involving most or all the dorsal and lumbar vertebrae. In 80 per cent the curvature was severe; many had "razor back" deformities.

Treatment applied. Myotomies, tenotomies, astraglectomies, Hoke stabilizations, arthrod-

eses, osteotomies of all types, leg lengthening, abdominal fascial reenforcements and spinal fusions were performed, and all attributed to use of limbs and security in standing and walking.

Results of spinal fusions. Eighty per cent failure was encountered in correcting the scoliosis or preventing increases. This may be attributed to delay in fusion, insufficient number of vertebrae fused and pseudoarthrosis in a few.

The prophylaxis of paralytic scoliosis includes (1) early recognition of deformity; (2) maintenance of symmetry of trunk; (3) support of the back by canvas corset, celluloid jacket, brace or plastic jacket; (4) reconstructive surgical treatment, which should be done as soon as the phase of spontaneous recovery has passed; (5) exercises, and (6) fascial reenforcement of the abdominal wall. This should be done early, as it has little if any value after severe scoliosis develops.

The treatment of scoliosis involves two features: (1) reduction of curvature, for which the author uses traction on the head and pelvis with the patient recumbent on a convex frame, and (2) spinal fusion, which should be contemplated as soon as scoliosis is discovered. Fusion should extend from the upper to the lower transitional vertebrae of the improved spine in a single curve or from the uppermost transitional vertebra to the lowermost in compound curves. Rest in bed (two to three months) should follow until fusion is solid. Then the back should be supported by a plastic jacket, corset or brace for several years.

Kleinberg<sup>252</sup> describes an extra-articular operation for correction of paralytic genu recurvatum. He employs two Steinmann pins for control of the fragments, one passed transversely through the distal end of the proximal fragment and the second one through the middle third of the tibia for control of the lower fragment. Osteotomy of the fibula is done 2 inches (5 cm.) below the neck, and the transverse osteotomy of the tibial shaft is done about 1½ inches (12.7 cm.) below the tubercle. The distal fragments are flexed; the upper fragments, maintained in hyperextension. A cast is applied incorporating both pins. Kleinberg summarizes the advantages of the procedure as follows:

1. The operative manipulation is completely extra-articular.

2. The surgery does not invade the knee joint and does not disturb its normal mechanism by taking away the patella.

251. Kleinberg, S.: Paralytic Scoliosis: An Analysis of Fifty-One Cases, *Am. J. Surg.* 64:301-312 (June) 1944.

252. Kleinberg, S.: The Operative Correction of Paralytic Genu Recurvatum, *Bull. Hosp. Joint Dis.* 5: 43-51 (April) 1944.

3. The technique does not use a bone graft in relation to the joint, and thus there is avoided friction of the bone against the articular condyles of the femur.
4. The operative procedure is relatively simple.
5. The re-establishing of the normal statics of the knee is accomplished by reversing the angulation of the metaphysis in a direction opposite to that of the acquired deformity and to approximately the same degree.
6. There is no disturbance of or interference with the musculature of the knee.

[Ed. NOTE.—I do not believe that Steinmann pins are necessary. Only one Kirschner wire is needed to maintain the upper fragment in hyperextension. If a tongue of bone is left attached to the lower fragment, the second pin is not necessary and one is assured of good bone contact and good apposition of the fragments. One important point that was not brought out is that genu recurvatum does not occur as a single deformity; there is usually some genu valgum and external torsion as well as the recurvatum deformity. All three deformities can be corrected at one procedure if after completing the transverse osteotomy one rotates the distal fragment in such a manner that the external torsion, genu valgum and genu recurvatum are corrected and then with a Gigli saw removes the appropriate wedge of bone from the distal fragment, the sawed surface being parallel with the cut surface of the upper fragment. A description of this procedure can be found in *The Journal of the American Medical Association* for Sept. 26, 1942.]

Mayer,<sup>253</sup> writing on the significance of the iliocostal fascial graft in the treatment of paralytic deformities of the trunk, describes three types. The deformities being classified according to the underlying muscle imbalance. In the first, there is a unilateral paralysis of all the muscles of the trunk. This produces a scoliosis with convexity to the paralyzed side and a downward tilt of the pelvis. This deformity leads to fixed pelvic obliquity. The second is due to the paralysis of external and internal oblique muscles, but the quadratus lumborum muscle remains normal, so that there is no pelvic obliquity. In the third type there is paralysis of abdominal muscles on both sides, producing a downward tilt of the pelvis and an exaggerated lumbar lordosis. He states that these deformities are not always clear-cut but that two of these classifications may be present in one deformity. He stresses the im-

portance of early detection of these deformities followed by early treatment which comprises "well leg traction," pulling down on the elevated side of the pelvis and pushing up on the depressed side. This "well leg traction" may or may not be combined with a Risser type of turnbuckle jacket. He describes in detail the iliocostal fascial transplant which passes from the crest of the ilium to the ninth rib on the same side. Spinal fusion alone is not adequate to control these deformities, because if the muscle imbalance is allowed to remain the scoliosis will promptly recur. Spinal fusion, however, is an important part of the treatment in correcting the three types of deformities he describes with which there is an exaggerated lumbar lordosis. It is not clearcut when a spinal fusion or a fascial graft should be combined. His rule is to do the fascial graft first and observe the patient at three month intervals, and if the scoliosis increases as much as 10 degrees then a spinal fusion should be done. He reports 38 cases in which forty-six grafts were done. The results were good or excellent in 30 cases.

[Ed. NOTE.—I cannot conceive of a fixed paralytic pelvic obliquity in the cases described under the first classification, wherein the deformity is confined to the trunk and can be corrected by fascial transplant alone. In these deformities the pelvis is not only oblique but displaced to one side. One must remember that a normal person when taking a step maintains the pelvis in a level position by the abductor muscles pulling down on the weight-bearing side, assisted by the lateral trunk groups pulling up on the opposite side, the femoral head being the fulcrum. When there is a paralysis of the trunk muscles on either side, this balanced system is disrupted. In all these cases there is a severe functional imbalance involving the side below the pelvic level on the side to which it is displaced and diagonally on the opposite side or trunk above the pelvic level. I have always done a Soutter fasciotomy to release the tight hip abductor muscles on the low side of the pelvis, followed by "well leg traction" in the attempt to restore the pelvis to its normal position. Then a fascial transplant is done on the same side. The pelvis cannot be restored to its original position in true fixed pelvic obliquity any more than one can completely correct the scoliosis with rotation. It is surprising how the walking of these persons is improved by simply doing a subtrochanteric osteotomy on the high side of the pelvis and shifting the femur nearer the midline.]

253. Mayer, L.: The Significance of the Iliocostal Fascial Graft in the Treatment of Paralytic Deformities of the Trunk, *J. Bone & Joint Surg.* 26:257-271 (April) 1944.

## X. POLIOMYELITIS

PREPARED BY J. A. TOOMEY, M.D., CLEVELAND

Paul<sup>254</sup> reports on the localization of the virus of poliomyelitis in human beings and on the epidemiology of the disease.

Howe and Bodian<sup>255</sup> demonstrated virus in a series of 174 specimens of stools from human beings and chimpanzees. They state that if 2 or more test animals were used the recovery rate would be 90 per cent.

Ward and Sabin<sup>256</sup> described 2 patients with poliomyelitis and 1 healthy person from whom poliomyelitis virus had been isolated from the stools in the winter.

Melnick<sup>257</sup> describes rod-shaped particles found with a new electron microscope in the stools of patients with poliomyelitis. They were also present in stools from normal patients; it was impossible to say whether these were the specific virus of poliomyelitis or were normal physiologic constituents of stools. Concrete evidence was lacking.

Howe and Bodian<sup>258</sup> isolated poliomyelitis virus from the stools of 2 uninoculated chimpanzees six months after they were quartered adjoining rhesus monkeys getting intranasal inoculation of potent human stools. They even demonstrated lack of antibody on admission and later development of antibody after isolation of virus from the stools.

Faber<sup>259</sup> and his associates produced poliomyelitis in monkeys (especially cynomolgus) with great facility, the route of the infection probably being by the afferent fibers of the fifth cranial nerve. Entry by way of sympathetic fibers of the nose and pharynx was also demonstrated in 1 instance. Faber believes that be-

cause of air and dirt contamination this may be a good source of infection.

Rendtorff and Francis<sup>260</sup> found virus in the abdomens of flies; presumably it does not multiply in the gastrointestinal tract. They also recovered it from fecal and vomit spots.

Rinehart<sup>261</sup> believes that there is a predisposing factor in the host which increases his susceptibility to poliomyelitis. He suggests salt depletion and hemoconcentrations as possible factors.

[ED. NOTE (J. A. T.).—One wonders why the disease is not more prevalent in the tropics and would agree further that more work needs to be done.]

Rosenow<sup>262</sup> believes that the inciting agent of poliomyelitis represents interrelated phases of the streptococcus and that the virus, as others term it, is the small filtrable invasive nonantigenic phase of the streptococcus.

In another communication, Rosenow<sup>263</sup> reports isolation of a filtrable infectious agent from neurotropic streptococci (the patient had hiccup) which first produced encephalitis and, after successive passages, symptoms and lesions of polioencephalitis in both mice and monkeys. The author believes that this is a "natural" poliomyelitis.

In a subsequent publication, Rosenow<sup>264</sup> brings together all of his experimental work on the filtrable invasive and nonantigenic phase of the streptococcus.

[ED. NOTE (J. A. T.).—One can say about all this work only that it does not seem to be accepted by persons working in the field, some of them claiming that they have tried to reproduce Rosenow's experiments, without results, and a few others confirming him. It appears that an unbiased study of this work is indicated.]

254. Paul, J. R.: Poliomyelitis, in Harvey Lectures, 1942-1943, Lancaster, Pa., Science Press, 1943, vol. 38, pp. 104-122.

255. Howe, H. A., and Bodian, D.: Efficiency of Intranasal Inoculation as Means of Recovering Poliomyelitis Virus from Stools, *Am. J. Hyg.* **40**:224-226 (Sept.) 1944.

256. Ward, R., and Sabin, A. B.: Presence of Poliomyelitis Virus in Human Cases and Carriers During Winter, *Yale J. Biol. & Med.* **16**:451-459 (May) 1944.

257. Melnick, J. L.: Detection with Electron Microscope of Rod-Shaped Particles in Stools of Normal and Poliomyelitic Individuals, *J. Immunol.* **48**:25-28 (Jan.) 1944.

258. Howe, H. A., and Bodian, D.: Poliomyelitis by Accidental Contagion in Chimpanzee, *J. Exper. Med.* **80**:383-390 (Nov.) 1944.

259. Faber, H. K.; Silverberg, R. J., and Dong, L.: Poliomyelitis in Cynomolgus Monkey: Infection by Inhalation of Droplet Nuclei and Nasopharyngeal Portal of Entry, with Note on This Mode of Infection in Rhesus, *J. Exper. Med.* **80**:39-57 (July) 1944.

260. Rendtorff, R. C., and Francis, T., Jr.: Survival of Lansing Strain of Poliomyelitis Virus in Common House-Fly, *J. Infect. Dis.* **73**:198-205 (Nov.-Dec.) 1943.

261. Rinehart, J. F.: Salt Metabolism in Poliomyelitis, *J. Nerv. & Ment. Dis.* **99**:825-833 (May) 1944.

262. Rosenow, E. C.: Poliomyelitis: Studies on Inciting Agent and Specific Serum Treatment, *Lancet* **1**:491-493 (April 15) 1944.

263. Rosenow, E. C.: Production of Filtrable Infectious Agent from Alpha Streptococci, *Am. J. Clin. Path.* **14**:156-167 (March) 1944.

264. Rosenow, E. C.: Poliomyelitis: Relation of Neurotropic Streptococci to Epidemic and Experimental Poliomyelitis and Poliomyelitis Virus: Diagnostic Serologic Tests and Serum Treatment, *Internat. Bu'l. Epizoot. M. Research & Pub. Hyg.* **A44**:9-83, 1944.

In three papers by Rosenow,<sup>265</sup> the same idea about the *Streptococcus* is expanded and encephalitis is considered as a kindred entity to poliomyelitis. He calls attention to the fact that only streptococci with neurotrophic properties inherent or induced will yield "neurotrophic" virus. He suggests that the relation between the streptococci and the virus in encephalitis and poliomyelitis is phasal rather than synergistic. In most instances the streptococci were of the alpha type. He describes a cutaneous reaction, a precipitation test, results of agglutination procedures and the other qualities of immunity and antigen sensitivity.

Milzer and colleagues<sup>266</sup> report that the Lansing strain of virus is inactivated in less than one second's exposure to ultraviolet rays and that the inactivated virus could be used as a vaccine to prevent the disease in monkeys and in mice.

[ED. NOTE (J. A. T.).—Before such a vaccine is tried, there is need for more and corroborative evidence.]

Meyer<sup>267</sup> believes that there is an inflammation of the walls of the jugular vein in patients with poliomyelitis, which responds promptly to the application of leeches over the inflamed jugular vein.

[ED. NOTE (J. A. T.).—There is no evidence to support this conception.]

Kramer, Geer and Szobel<sup>268</sup> tested the effects of innumerable agents for their viricidal activity—so far as barbiturates, dyes, organometallic compounds, sulfonamide compounds and a host of chemicals (one hundred and sixty items in all) were employed, with negative results.

[ED. NOTE (J. A. T.).—This is an important and fundamental piece of work.]

265. Rosenow, E. C.: Filterable Infectious Agent Obtained from Alpha Streptococci Isolated in Studies of Case of Poliomyelitis, *Am. J. Clin. Path.* **14**:519-533 (Oct.) 1944; Specific Streptococcal Antibody-Antigen Reactions in Poliomyelitis: Preliminary Report, Proc. Staff Meet., Mayo Clin. **19**:444-448 (Aug. 23) 1944; Studies on Virus Nature of Infectious Agent Obtained from Four Strains of "Neurotropic" Alpha Streptococci, *J. Nerv. & Ment. Dis.* **100**:229-262 (Sept.) 1944.

266. Milzer, A.; Oppenheimer, F., and Levinson, S. O.: Production of Potent Inactivated Vaccines with Ultraviolet Irradiation: Abbreviated Preliminary Report on Completely Inactivated Vaccine (Lansing Strain Virus) in Mice, *J. A. M. A.* **125**:704-705 (July 8) 1944.

267. Meyer, O.: New Principle in Treatment of Poliomyelitis, *Internat. Bull. M. Research & Pub. Hyg.* **A44-P**:5-9, 1944.

268. Kramer, S. D.; Geer, H. A., and Szobel, D. A.: Chemoprophylactic and Therapeutic Action of Wide Variety of Chemical Compounds on Two Neurotropic Virus Infections in Mice, *J. Immunol.* **49**:273-314 (Nov.) 1944.

Toomey<sup>269</sup> believes that sulfonamide compounds should not be given to patients with poliomyelitis, since experiments show an aggravation of the disease when these drugs are given to experimental animals.

Ehrich and Foster<sup>270</sup> repeated histologic studies of mouse poliomyelitis and found it to be the same as that described by Lillie, Armstrong, Jungeblut and Sanders. There is good correlation between the histologic changes in the central nervous system and the clinical signs.

Jungeblut<sup>271</sup> showed that two strains of human poliomyelitis virus and Theiler's mouse encephalomyelitis virus revealed overlapping in cross neutralization and in antiviral immune serum tests, reciprocal in some but not so in others. He obtained evidence of group specificity after intracerebral tests and of strain specificity after intraperitoneal tests. He believes that all virus previously referred to could be classed under a "poliomyelitis group."

Paul<sup>272</sup> found that grivet and vervet monkeys are more susceptible to poliomyelitis virus than are baboons, and he feels that they are satisfactory animals to work with in experimental poliomyelitis.

Rasmussen and colleagues<sup>273</sup> showed that mice fed an adequate diet save for various levels of riboflavin showed no consistent differences to infection with Theiler's virus. In experiments with the Lansing strain, there was slight but definitely greater resistance in the deficient group.

McCormick<sup>274</sup> has for a long time been of the opinion that thiamine deficiency has something to do with poliomyelitis and that there is an affinity between beriberi and poliomyelitis.

Lichstein and co-workers<sup>275</sup> showed that mice fed rations deficient only in calcium pantothenate have increased resistance to Theiler's encephalitis but the course of the disease following infection with the Lansing virus is not influenced.

269. Toomey, J. A.: Treatment of Poliomyelitis, *J. A. M. A.* **126**:49 (Sept. 2) 1944.

270. Ehrich, W. E., and Foster, C.: Experimental Poliomyelitis in Mice: Observations on Its Genesis and on Histologic Changes, *Arch. Path.* **38**:365-369 (Dec.) 1944.

271. Jungeblut, C. W.: Serologic Relationships Within Poliomyelitis Group of Viruses, *Am. J. Pub. Health* **34**:259-264 (March) 1944.

272. Paul, J. R.: Susceptibility of East African Monkeys to Experimental Poliomyelitis, *Yale J. Biol. & Med.* **16**:461-466 (May) 1944.

273. Rasmussen, A. F., Jr.; Waisman, H. A., and Lichstein, H. C.: Influence of Riboflavin on Susceptibility of Mice to Experimental Poliomyelitis, *Proc. Soc. Exper. Biol. & Med.* **57**:92-95 (Oct.) 1944.

(Footnotes continued on next page)

[ED. NOTE (J. A. T.).—One wonders about such results when it is learned that the virus was introduced intracerebrally.]

Foster and colleagues<sup>276</sup> enlarge on their theory that a thiamine deficiency protects, and they now show that the protection is not due to a resulting anorexia.

Weaver and colleagues<sup>277</sup> report that the result of their experiments on cotton rats yielded no evidence that avitaminosis D partial inanition and other factors altered the susceptibility of their cotton rats to the Armstrong Lansing strain of poliomyelitis virus. It is felt that their conclusions were justified as regards rats. They mention Toomey's experience with vitamin D-deficient animals.

[ED. NOTE (J. A. T.).—It is only fair to point out that Weaver and co-workers used rats, animals which do not acquire rickets from the exclusion of the vitamin D factor but contract the disease only when the calcium-phosphorus ratio is disturbed by an unbalanced diet, a condition which vitamin D alone does not cure. Weaver's work did not repeat Toomey's experiments—experiments in which the virus was introduced by way of the gastrointestinal tract into monkeys, animals susceptible to vitamin D deficiency.]

Toomey and associates<sup>278</sup> were unable to acclimate virus to white rats either overfed or deficient in vitamin B. They confirmed the point raised by Foster and colleagues that there is a difference between vitamin B-deficient animals and overfed or sufficiently fed animals. However, these workers thought that the difference might not be so striking if, despite lack of paralysis, the presence of virus could be demonstrated in the animals that died. When second generation transfers were made with cords of mice that died without paralysis in the

first generation, there was no significant difference in the total number of animals paralyzed in the vitamin B-overfed and the vitamin B-deficient groups of animals. These authors suggest that a conclusion the reverse of the usual one could be made, in that in mice overfed with thiamine some slight protection developed and that the development of paralysis in these animals might indicate a slight protection to the virus.

Rasmussen and associates<sup>279</sup> felt that they as had Foster and co-workers, had proved the mice fed low caloric diets deficient in thiamine showed a lower incidence of infection both to Theiler's and to Lansing's strains of virus. In some thiamine-deficient survivors subsequently given adequate thiamine, paralysis occurred after a prolonged incubation period.

In brief, Foster and colleagues<sup>280</sup> showed that there was more paralysis following injection of Lansing poliomyelitis in mice given more thiamine hydrochloride than in those that had deficiency.

[ED. NOTE (J. A. T.).—Though there was statistical difference, one wonders whether the statement can be made that deficiency increases resistance.]

Marshall<sup>281</sup> makes an attempt to implicate vitamin C as a factor in the poliomyelitis concept.

[ED. NOTE (J. A. T.).—His evidence and authorities quoted do not prove his point.]

Frohring and Toomey<sup>282</sup> showed that in 14 patients with poliomyelitis the biotin content was about 20.6 micrograms, the riboflavin content between 500 and 800 micrograms and the pantothenic acid content between 1,460 and 6,760 micrograms. The biotin and riboflavin contents seemed higher than the figures obtained by other investigators for normal persons.

Wood<sup>283</sup> cites some examples as to how possible reaction might be thrown out of balance

274. McCormick, W. J.: Pathologic Affinities of Beriberi and Poliomyelitis, *M. Rec.* 157:414-419 (July) 1944.

275. Lichstein, H. C.; Waisman, H. A.; Elvehjem, C. A., and Clark, P. F.: Influence of Pantothenic Acid Deficiency on Resistance of Mice to Experimental Poliomyelitis, *Proc. Soc. Exper. Biol. & Med.* 56:3-5 (May) 1944.

276. Foster, C.; Jones, J. H.; Henle, W., and Dorfman, F.: Comparative Effects of Vitamin B<sub>1</sub> Deficiency and Restriction of Food Intake on Response of Mice to Lansing Strain of Poliomyelitis Virus, as Determined by Paired Feeding Technic, *J. Exper. Med.* 80:257-264 (Oct.) 1944.

277. Weaver, H. M.: Effect of Rachitogenic Diets, Partial Inanition, and Sex on Resistance of Cotton Rats to the Virus of Poliomyelitis, *J. Pediat.* 24:88-105 (Jan.) 1944.

278. Toomey, J. A.; Frohring, W. O., and Takacs, W. S.: Vitamin B<sub>1</sub> Deficient Animals and Poliomyelitis, *Yale J. Biol. & Med.* 16:477-485 (May) 1944.

279. Rasmussen, A. F., Jr.; Waisman, H. A.; Elvehjem, C. A., and Clark, P. F.: Influence of Level of Thiamine Intake on Susceptibility of Mice to Poliomyelitis Virus, *J. Infect. Dis.* 74:41-47 (Jan.-Feb.) 1944.

280. Foster, C.; Jones, J. H.; Henle, W., and Dorfman, F.: The Effect of Vitamin B<sub>1</sub> Deficiency and of Restricted Food Intake on the Response of Mice to Lansing Strain of Poliomyelitis Virus, *J. Exper. Med.* 79:221-234 (Feb.) 1944.

281. Marshall, R.: Physiological Paralysis Protection, *M. Rec.* 157:281-284 (May) 1944.

282. Frohring, W. O., and Toomey, J. A.: Riboflavin, Pantothenic Acid and Biotin Excretion Tests in Patients with Paralytic Poliomyelitis, *J. Pediat.* 24:293-294 (March) 1944.

283. Wood, H. G.: Metabolism of Nervous Tissue in Poliomyelitis, *Journal-Lancet* 64:240-242 (July) 1944.

by interference of a virus and thus upset cellular metabolism. The reported interference of poliomyelitis with the anaerobic glycolysis of the brain has not been confirmed.

Nickle and Kabat<sup>284</sup> claim some specific differences in metabolism between brain tissue infected with Western equine encephalomyelitis and that infected with poliomyelitis. Utilization of oxygen of the poliomyelitic brain is below normal with a glucose concentration of 121 mg. per hundred cubic centimeters; with a concentration of 217 mg. per hundred cubic centimeters utilization of oxygen of the encephalitic brain is below normal, but that of the poliomyelitic brain is not. Other substrates were used to show a difference, lactate-glucose, pyruvate-glucose and succinate-glucose.

Gellhorn<sup>285</sup> reports investigations on the influence of muscle pain on muscular incoordination. He concludes that movements are modified in intensity and equality not only by proprioceptive impulses but also by muscle pain.

Kabat and colleagues<sup>286</sup> report a decrease in the lactic acid content of the brains of mice infected with poliomyelitis virus. They feel that this evidence supports the view that the virus may interfere with metabolism.

Carey's publication<sup>287</sup> is fundamental and describes the early histologic changes that occur in the neuromuscular mechanism of experimental poliomyelitis in monkeys. The early loss of the motor end plate was striking. He suggests tentatively that the changes are a result of abnormal excitation of the secretory mechanism of motor end plates which results in progressive exhaustion of the gold-staining axonic substance leading to denervation at the myoneural junction.

Gard<sup>288</sup> describes two colonies of albino mice in which, during epizootics caused by *Salmonella enteritidis* and *Bacillus piliformis*, there were 4 and 5 cases of spontaneous mouse poliomyelitis observed. The transfers were easiest when made from the intestine, next easiest from the lymph nodes and then from the tissue of the

central nervous system. The involvement of the lymph node was stressed.

Herrarte and Francis<sup>289</sup> described several methods of recovering virus from various biologic specimens.

Bourdillon<sup>290</sup> studied the sedimentation, the electrophoretic mobility and the serologic reactivity of purified Jungeblut's SK adapted mouse strain in its two hundred and seventieth to three hundred and twentieth passage. The injected dose was always 0.03 cc. of serial dilutions.

[ED. NOTE (J. A. T.).—The article is a technical one; suffice it to say that it is one not well suited for abstract.]

Foster and Ehrich<sup>291</sup> describe the technics which they used to demonstrate the alterations of brain and spinal cord characterizing infection with Lansing strain of virus in the mouse.

Bourdillon<sup>292</sup> describes in detail the methods of purification of virus by means of the Swedish angle centrifuge.

A long article on the therapy of poliomyelitis in the acute stages of the disease has been written by Toomey.<sup>293</sup> He concludes:

1. As first shown by Feiss, immobilization and splints are unnecessary in the acute stages of poliomyelitis.

2. Active movement, manipulations, etc., in the acute stage of the disease do not harm the patient.

3. Some form of heat should be used to bring about vascular dilatation in the early stages of the disease. The muscles should be moved through their normal arcs.

4. Muscle reeducation plays the most important role in poliomyelitis therapy. It should be started early and should be persistently carried out over a long period of time.

An excellent article by Ward<sup>294</sup> is devoted to the epidemiology of poliomyelitis. He gives a good review of the probable epidemiologic facts known to date.

289. Herrarte, E., and Francis, T., Jr.: Efforts Toward Selective Extraction of Poliomyelitis Virus, *J. Infect. Dis.* **73**:206-211 (Nov.-Dec.) 1943.

290. Bourdillon, J.: Purification, Sedimentation, and Serological Reactions of the Murine Strain of SK Poliomyelitis Virus, *Arch. Biochem.* **3**:285-297 (Feb.) 1944.

291. Foster, C., and Ehrich, W. E.: Demonstration of Lesion Produced by Experimental Poliomyelitis in Central Nervous System of Mouse, *Arch. Path.* **37**:264-271 (April) 1944.

292. Bourdillon, J.: Heat Inactivation of Murine Strain of SK Poliomyelitis Virus, *Arch. Biochem.* **3**:299-303 (Feb.) 1944.

293. Toomey, J. A.: Observations on Treatment of Infantile Paralysis in Acute Stage (Nathan Lewis Hatfield Lecture), *Tr. & Stud., Coll. Physicians, Philadelphia* **12**:14-25 (April) 1944.

294. Ward, R.: The Epidemiology of Poliomyelitis, *J. Bone & Joint Surg.* **26**:829-832 (Oct.) 1944.

284. Nickle, M., and Kabat, H.: Specificity in Effects on Brain Metabolism of Two Differing Neurotropic Viruses, *J. Exper. Med.* **80**:247-255 (Sept.) 1944.

285. Gellhorn, E.: Effect of Muscle Pain on Central Nervous System at Spinal and Cortical Levels, *Journal-Lancet* **64**:242-245 (July) 1944.

286. Kabat, H.; Erickson, D.; Eklund, C., and Nickle, M.: Decrease in Lactic Acid Content of Brain in Poliomyelitis, *Science* **98**:589-591 (Dec. 31) 1943.

287. Carey, E. J.: Study on Ameboid Motion and Secretion of Motor End-Plates: Anatomic Effects of Poliomyelitis of Neuromuscular Mechanism in Monkey, *Am. J. Path.* **20**:961-995 (Sept.) 1944.

288. Gard, S.: Observations Concerning the Pathogenesis and the Epidemiology of Mouse Poliomyelitis, *Yale J. Biol. & Med.* **16**:467-476 (May) 1944.

## XI. POLIOMYELITIS: CONVALESCENT TREATMENT AND RELATED SUBJECTS

PREPARED BY ROBERT L. BENNETT, M.D., WARM SPRINGS, GA.

The following articles concerning the treatment of patients in the convalescent phase of acute anterior poliomyelitis will be divided into five parts:

1. Articles on the natural course of poliomyelitis, when no treatment is given.
2. Articles on the purposes, the techniques and the results of the so-called orthodox treatment.
3. Articles on the purposes, the techniques and the results of the Kenny method of treatment.
4. Articles on the purposes, the techniques and the results of combination forms of treatment.
5. Articles on subjects having a direct bearing on treatment.

*The Natural Course of Poliomyelitis.*—Sherman<sup>295</sup> reports her observations on a group of 70 unselected patients through the entire course of their acute disease and through the first six months of the convalescent phase. The patients received the same general treatment as that essentially required for any acute febrile condition. They were given absolute rest in bed, with as nearly a normal diet as possible, and were disturbed only for rapid physical examinations. Fifty-three of the patients received convalescent, or adult blood serum. Kenny packs, splints or special apparatus were not used. Patients were discharged as soon as convalescent, even though the period of quarantine had not expired. Of the 70 patients, 13 (18.5 per cent) were nonparalytic; 9 (13 per cent) had only bulbar involvement, and the remaining 48 (68.5 per cent) had spinal or bulbospinal involvement. Six patients (8.6 per cent) died. At the end of six months, 38 (54.3 per cent) patients who had demonstrable weakness during the acute phase were not handicapped. Of these, 7 (10 per cent) had no detectable weakness and 31 (44.2 per cent) had functionally insignificant weakness. Six (8.6 per cent) had functionally significant weakness but required no therapy, and 7 (10 per cent) had severe weakness requiring braces or surgical treatment.

Hipps and Crook<sup>296</sup> report on a study of 88 patients observed over a period of two and a half years. These patients were divided into three groups: (1) patients treated by rest, splints and plaster casts early in the course of the disease; (2) patients given physical therapy

under water early in the course of the disease and (3) patients who were given no treatment. In the group in which no treatment was given there was 31.1 per cent improvement. In the group in which early rest, splints and plaster casts were used, there was 33.8 per cent improvement. In the group in which early physical therapy under water was given, 68.5 per cent improvement was noted.

*Orthodox Treatment.*—Hipps and Crook in presenting the aforementioned 88 patients give in detail the early type of treatment given the patients brought to the hospital soon after onset of the disease and given treatment under water immediately. This treatment consisted in immersing the patient in a pool supplied with flowing hot salt water and kept constantly at a temperature of 98.6 F. The child was carried to the pool on a canvas stretcher and supported in the pool by this stretcher. Gentle under water massage was given the muscles until soreness was too intense. As soon as the soreness began to disappear and the child felt that he could or wanted to try movement, a physical therapist assisted him in the arc of motion. Actual muscle reeducation was started as soon as soreness and articular limitation permitted.

Toomey and Kohn<sup>297</sup> report results of treatment of 226 patients during the years 1931 and 1942. They present a program of care that Toomey has used for many years. They make the statement that patients should not walk unless they walk correctly, that gait should be synchronous and against gravity without a limp and without any added jerking movement that would denote substitution of muscles. Orthopedic devices should be used to support muscles and coordinate movement when the patient becomes active. They further say that "percentage of patients who will be referred to orthopedic surgeons in the future will be about the same as in the past, but the patients will be in a better condition to profit by orthopedic aid."

Key<sup>298</sup> outlines his concept of treatment of infantile paralysis during the acute stage, the stage of tenderness and contracture, the convalescent stage and the chronic stage. His treatment is essentially good supportive care during the acute stage and protection of

<sup>295</sup> Sherman, M. S.: The Natural Course of Poliomyelitis, *J. A. M. A.* **125**:99-102 (May 13) 1944.

<sup>296</sup> Hipps, H. E., and Crook, B. L.: Early Treatment of Infantile Paralysis, *Arch. Phys. Therapy* **25**: 439-47 (July) 1944.

<sup>297</sup> Toomey, J. A., and Kohn, P. M.: Poliomyelitis: Results of Treatment During the Acute Stage of Disease, *Am. J. Dis. Child.* **67**:393-399 (May) 1944.

<sup>298</sup> Key, J. A.: The Treatment of Infantile Paralysis, *J. Missouri M. A.* **41**:70-73 (April) 1944.

involved segments by immobilization in splints or casts in a neutral position during the stage of tenderness or contracture. In order to prevent stiffness, the splints and casts are removed once or twice a day and the joints moved passively through as great an arc as can be tolerated by the patient. In the convalescent stage, splints or casts are removed and the patient is encouraged to move about in bed and exercise his limbs in order to loosen up the muscles and joints. Once or twice a day he is placed in a tub of warm water and the paralyzed limbs are exercised. Muscle training preferably is carried out by skilled physical therapists, but the mother or a nurse may be taught to carry on the prescribed treatment for a given patient in a satisfactory manner. In the chronic stage, orthopedic apparatus is used to prevent deformities and improve function of paralyzed segments. Key states:

This is the orthodox treatment and when it is properly carried out approximately 80 per cent of the patients who develop infantile paralysis during an epidemic may be expected to recover to a point at which they are normal or practically normal. About 20 per cent will be crippled permanently to a variable degree, but only about 1 per cent will be crippled so severely that they will become wheel chair cases.

These figures are from three recent epidemics. Key also states that he does not approve of the Kenny method and enumerates sixteen reasons why he does not.

Scott and Rountree<sup>299</sup> report on 46 cases which occurred during the period from March to November 1941. Thirty-nine patients had or contracted paralysis shortly after admission to the hospital. Thomas splints and Bradford frames were used for all patients. At the end of two years, accurate follow-up studies were made on 39 of the 46 patients. There were 3 (7.7 per cent) deaths. Nine patients (23 per cent) made a complete recovery. Twelve (30.7 per cent) were released from treatment, and 15 (38.4 per cent) were still under treatment. Of the 12 released from treatment, 7 were able to walk without appliances, 3 were able to walk with appliances and 2 were unable to walk. Of the 15 still under treatment, 8 were able to walk without appliances and 3 with appliances and 4 were unable to walk. "The results of the treatments used are not encouraging."

*Kenny Method of Treatment.*—O'Connor<sup>300</sup> gives the history of the Kenny method, out-

lining the aid given to Kenny by the National Foundation for Infantile Paralysis, Inc.

Kenny<sup>301</sup> presents and answers two questions: first, concerning her concept of the disease, acute anterior poliomyelitis, and, second, concerning the treatment for this concept. As evidence of the value of her treatment over "orthodox treatment," she presents first the report of McCarroll (*J. A. M. A.* 120:517-519 [Oct. 17] 1942) and contrasts this report with that of Bingham (*J. Bone & Joint Surg.* 25: 647-650 [July] 1943). Kenny feels that her answers given in the latter article substantiate the claim that her contribution is not a treatment for recognized symptoms but an entirely new concept of the disease itself.

Knapp<sup>302</sup> presents his observations on the symptoms and treatment of poliomyelitis. He makes the statement that "Muscle shortening is a positive entity in infantile paralysis and is an important factor in the final function end-result." He states that "'mental alienation' is probably only a minor factor in infantile paralysis and is probably not psychologic in origin as thought by Miss Kenny." Maximum efficiency of muscle function within the limits imposed on it by denervation is the aim of treatment and the explanation for the good results obtained.

[ED. NOTE.—Dr. Knapp in this article presents his own opinion of the symptoms and treatment. It is worth while to read of this treatment and the article of Kenny mentioned. As is well known, Kenny and Knapp have worked together since Kenny's first visit to the United States, in 1940.]

Ghormley and colleagues<sup>303</sup> present a report of the committee for the investigation of the Kenny treatment of poliomyelitis, following a resolution passed by the Section on Orthopedic Surgery of the American Medical Association. This committee visited a total of six cities and sixteen clinics. A total of approximately 740 patients were examined. Approximately 650 of these patients had been treated by the method advocated by Miss Kenny. The report discusses four major points of the concept of the disease and outlines the major points of the Kenny treatment. Each of the points outlined was

301. Kenny, E.: *Kenny Treatment of Poliomyelitis*. Proc. Interst. Postgrad. M. A. North America (1942). 1943, pp. 312-316.

302. Knapp, M. E.: *Observations on Infantile Paralysis*, *Journal-Lancet* 64:164-168 (May) 1944.

303. Ghormley, R. K., and others: *Evaluation of the Kenny Treatment of Infantile Paralysis*, *J. A. M. A.* 125:466-469 (June 17) 1944; *Evaluation of the Kenny Treatment of Infantile Paralysis*, *Arch. Phys. Therapy* 25:415-420 (July) 1944.

299. Scott, E. B., and Rountree, G. R.: *A Study of Forty-Six Cases of Poliomyelitis, Kentucky M. J.* 42: 182-184 (June) 1944.

300. O'Connor, B.: *The Story of the Kenny Method*, *Arch. Phys. Therapy* 25:231-234 (April) 1944.



analyzed and discussed. Outstanding in the final comments of the committee are the following:

1. "Miss Kenny's objection to muscle examination and hence the lack of accurate records is to be condemned."

2. Miss Kenny's statement that under orthodox treatment only 13 per cent of the patients recovered without paralysis while under the Kenny method over 80 per cent recovered is a "deliberate misrepresentation of the facts of treatment by other methods."

3. The Kenny method "does not prevent or even minimize the degree of permanent paralysis."

4. The claim by many of those who have used the Kenny method that all paralytic scoliosis can be prevented is open to question, because several more years must elapse before any final conclusions can be reached with regard to amelioration or prevention of paralytic scoliosis by means of the Kenny method.

5. The committee acknowledges that the wide publicity pertaining to the Kenny method has stimulated the medical profession to reevaluate known methods of treatment of this disease and to treat it more effectively.

Gill<sup>304</sup> presents an interpretation of the Kenny concept and treatment of infantile paralysis. He makes this statement:

It is evident, therefore, that the Kenny methods of treatment are very similar to the orthodox methods, and in many particulars identical with them in spite of the different terminology employed by Miss Kenny. The statement that the two methods have nothing in common displays an ignorance of the orthodox methods.

In general, Gill points out, what is new in the Kenny methods is not particularly good and what is good is not particularly new.

Ransohoff<sup>305</sup> presents results in 33 cases occurring in the epidemic of 1942 and observed through June 1943. In this series of cases, there were 4 (12.1 per cent) deaths; in 1 case (3.3 per cent) there was no follow-up; 7 patients (21.2 per cent) had severe residual paralysis, and 12 (39.3 per cent) were "completely cured." Thus, 21 patients (63.5 per cent) returned to normal or were without functional handicap. Ransohoff makes the statement that the cost of the Kenny treatment is "tremendous" and is "five times as expensive as the orthodox."

304. Gill, A. B.: The Kenny Concept and Treatment of Infantile Paralysis, *J. Bone & Joint Surg.* 26: 87-98 (Jan.) 1944.

305. Ransohoff, N. S.: Experiences with the Kenny Treatment for Acute Poliomyelitis in the Epidemic of 1942, Monmouth and Ocean Counties, New Jersey, *J. Bone & Joint Surg.* 26:99-102 (Jan.) 1944.

Barnett<sup>306</sup> reports on the treatment of 1 patients during the epidemic in Sonoma County, Calif. There was no note of division of patients according to the various types of poliomyelitis but the conclusion was made that all but 8 per cent of the patients were eventually functionally normal or nearly so and only 2 per cent were seriously involved. The claim is made that patients were more comfortable after two weeks of the disease and better physically with this type of treatment than patients after three months with the old type of therapy.

Horan<sup>307</sup> outlines the Kenny treatment but gives no results. He makes the statement that the Kenny treatment requires much more work than the orthodox. With the older type of treatment, one nurse could easily care for 5 to 10 patients, but the "Kenny method requires 4 to 5 nurses to look after one patient."

Frankel<sup>308</sup> reports on a year's observation of 6 cases. He makes the statement, "If it [Kenny method] only offers the patients greater comfort than the Orthodox therapy and does no harm, it is worthwhile."

Yount<sup>309</sup> outlines the Kenny method but gives no results of the treatment are given. She discusses the Kenny concept in detail.

Bohnengel<sup>310</sup> discusses the psychobiologic factors in the care of poliomyelitis in the past and present. He makes the following statement:

The crux of the whole controversy over the Kenny concept lies in the fact that one group of observers principally the Minneapolis group, is using psychobiologic methods of observation, experimentation and treatment and therefore brings into view only those phenomena which exist at the psychobiologic level (organismic integration). The other group, using more purely physical methods of study, brings into its field of vision only those phenomena which exist at the anatomic-physiologic level of organismic integration. Both groups tend to lose sight of the fact that the two symptoms may be coexistent not only in the same individual but in the same muscle.

*Combined Forms of Treatment.*—Boines<sup>311</sup> reports on the use of neostigmine and a modified

306. Barnett, E. D.: A Recapitulation on One Poliomyelitis Siege with Some Notes on Hot Pack Therapy, *Hospitals* 18:39-41 (Sept.) 1944.

307. Horan, W. A.: Kenny Treatment of Poliomyelitis, *Rhode Island M. J.* 27:16-18 (Jan.) 1944.

308. Frankel, C. J.: The Kenny Treatment for Infantile Paralysis—A Year's Observation of Six Cases, *Virginia M. Monthly* 71:79-83 (Feb.) 1944.

309. Yount, F.: New Developments in the Study of Poliomyelitis, *Arizona M. J.* 1:61-64 (March-April) 1944.

310. Bohnengel, C.: Psychobiologic Factors in the Kenny Concept of Infantile Paralysis, *Arch. Phys. Therapy* 25:350-356 (June) 1944.

311. Boines, G. J.: The Use of Prostigmine and a Modified Kenny Technique in the Treatment of Poliomyelitis, *J. Pediat.* 25:414-433 (Nov.) 1944.

and Kenny technic. Of the 21 cases, there were good to excellent end results in all. The modification of the Kenny technic consisted in the limitation of hot packs and the substitution of prostigmine, usually orally but occasionally parenterally as well. No change was made in the usual methods of muscle reeducation of or in the passive joint movement procedure. He states, "Approximately 75 per cent of patients with poliomyelitis can be adequately cared for at home without special nursing attention with this technique." Boines also urges the extension of this method of therapy especially in chronic cases. McFarland and colleagues<sup>312</sup> make a preliminary report of a series of 74 selected cases in which neurotripsy was combined with the Kenny treatment. In 25 of these cases neurotripsy was done while the Kenny treatment was being given in the acute stage, and in 49 cases of longstanding residual paresis neurotripsy also was done in combination with the Kenny method. The rationale of neurotripsy is the fact that in regrowth after nerve interruption there is an increased branching. The authors present an outline of the procedure, which is done with general or spinal anesthesia with the objective of breaking as many branches of the remaining motor nerve axons as possible. The technic is to knead through the muscle vigorously and deeply with a blunt instrument. The muscle is covered thoroughly throughout its entire extent. There has been a rather consistent increase in circulation in the involved segments, and an increase in muscle size is a "frequent result." Improvement in muscle strength occurred in over one half of one hundred and thirty muscle groups studied. "The results are encouraging."

Miley<sup>313</sup> presents a preliminary report on 58 cases in which the Knott technic of ultraviolet irradiation of blood was used in addition to the Kenny treatment. There were no harmful effects in this series of cases. This technic did not interfere with the Kenny routines. No attempt was made to evaluate the ultimate end results for these patients, but it is Miley's conclusion that further extensive clinical studies with this combination of treatments is warranted.

Nelson<sup>314</sup> discusses the present status of poliomyelitis. Regarding treatment, he says that hot

packs during the stage of spasm followed by muscle reeducation offer the most help in the acute stages.

Compere<sup>315</sup> outlines the management and care of patients with infantile paralysis. He states that his own observation led to the conclusion that the earlier the program of treatment of peripheral manifestations is done the better are the end results. Microscopic sections of muscles that are in spasm show a picture of pathologic congestion. This congestion may be relieved by hot packs, passive motion and active exercise. He further concludes that the number of patients who will require surgical intervention may be as large as that of the patients who have received other types of treatment but that the patients given treatment by hot packing, early activity, exercises and good physical therapy will be in better condition generally and will thus obtain greater profit from the efforts of the orthopedic surgeon.

Wright<sup>316</sup> presents problems encountered in the early treatment of poliomyelitis. She states that Kenny has made a valuable contribution but that one will continue to use to advantage the Silver method of the prevention of stasis of the circulation by special postural measures in bed, the Lovett-Merrill method of muscle testing, the Kendall percentage grading, the Lowman under water reeducation and the light, efficient supports when indicated. In a second article, Wright<sup>317</sup> outlines a reasonable program of treatment for acute poliomyelitis. She notes that "treatment can not be by one method only but must meet the needs of each case."

Wolf<sup>318</sup> in discussing the clinical aspects of poliomyelitis, states that "when a patient with pure bulbar poliomyelitis is placed in a respirator it can be seen that more harm than good results. The patient breathes with the machine at times and against it at others. The use of the respirator under these conditions may be extremely harmful."

Thompson<sup>319</sup> discusses the Kenny method and correlates a program of occupational therapy combined with the Kenny method.

315. Compere, E. L.: Management and Care of the Infantile Paralysis Patient, *Arch. Phys. Therapy* **24**: 709-712 (Dec.) 1943.

316. Wright, J.: Problems in Early Treatment of Poliomyelitis, *New York State J. Med.* **44**:67-72 (Jan. 1) 1944.

317. Wright, J.: Reasonable Treatment of Acute Poliomyelitis, *Pub. Health Nursing* **36**:510-515 (Oct.) 1944.

318. Wolf, A. M.: Symposium on the Management of Poliomyelitis, *Am. J. Dis. Child.* **67**:332-334 (April) 1944.

312. McFarland, J. W.; Billig, H. E., Jr.; Taylor, G. M., and Dail, C. W.: Kenny Treatment Combined with Neurotripsy in Care of Poliomyelitis, *Arch. Phys. Therapy* **25**:645-650 (Nov.) 1944.

313. Miley, G.: Ultraviolet Blood Irradiation Therapy in Acute Poliomyelitis, *Arch. Phys. Therapy* **25**: 651-656 (Nov.) 1944.

314. Nelson, N. B.: Poliomyelitis: Its Present Status, *California & West. Med.* **60**:18-21 (Jan.) 1944.

*Additional Reports Bearing on Treatment.*—Kabat and Knapp<sup>320</sup> present the "internuncial cell theory" of the mechanism of muscle spasm. They discuss muscle spasm in detail and present evidence to support the theory that the pathologic basis of muscle spasm in poliomyelitis is a lesion of internuncial neurons in the gray matter of the spinal cord. With damage to these cells, the muscle spasm is produced as a result of the release of proprioceptive reflexes from inhibition. They support this theory by animal experimentation, by the study of pathologic changes in the spinal cord in 68 cases of poliomyelitis in human beings, by measurement of chronaxia of muscles in 14 patients and by the use of neostigmine acting on the spinal cord to inhibit proprioceptive reflexes.

Bouman and Schwartz<sup>321</sup> discuss muscle spasm and demonstrate its existence by means of action currents. They state that the motor neuron receives three separate groups of impulses: (1) impulses which give rise to voluntary contraction; (2) inhibitory impulses, and (3) excitatory impulses from the reflex arcs. They feel that if only the excitability to inhibitory impulses is gone the motor unit innervated by the particular neuron will show spasticity but no decrease in voluntary function. If both the inhibitory and the voluntary impulses are no longer able to excite the motor neuron, spasticity will be present, while the muscles will show decreased function, and, finally, when all motor neurons have lost the excitability to all three types of impulses both voluntary contraction and spasticity of muscles will disappear.

Schwartz and colleagues<sup>322</sup> present the etiology, pathogenesis and significance of muscle spasm in acute poliomyelitis, to bring out the fact that evidence of spasticity has been recorded from (a) weakened muscles; (b) antagonists of weakened muscles, and (c) muscles which exhibit no clinical or other evidence of weakness. They feel that spasticity and weakening are two separate phenomena, each dependent on specific disturbances of the anterior horn cells. They further feel that there is every indication that

spasm runs its course like other clinical manifestations of the disease.

Moldaver,<sup>323</sup> in an analysis of the neuromuscular disorders in poliomyelitis, brings out the fact that paralytic and parietic muscles, called "alienated" under the Kenny concept of the disease, always show some degree of neuromuscular degeneration. The extent of this degeneration can be shown by chronaxia determinations. It is his opinion that there are three major causes of spasm: (1) meningeal irritation; (2) shortening of uninvolved antagonistic muscles, and (3) inflammation of the posterior root ganglion.

McFarland and Graves<sup>324</sup> outline a method of recording muscle spasm in the acute stage of infantile paralysis and the degree of tightness or contracture present in the convalescent stage.

Gurewitsch and O'Neill<sup>325</sup> analyze a group of 513 children between the ages of 4 and 10 years. These children were given five simple flexibility tests. The performances were found to vary widely. The authors emphasize that constitution, heredity and sex are factors in normal flexibility, and they suggest that caution be used in the interpretation of limited flexibility encountered in patients during convalescent stages of poliomyelitis.

Hall and colleagues<sup>326</sup> state that hot packs applied to muscles temporarily decrease the power of voluntary contraction about 10 per cent.

Stevenson<sup>327</sup> discusses the problem of public health nursing as it was demonstrated in the 1943 epidemic of poliomyelitis.

Draper<sup>328</sup> presents a statewide emergency plan to care for an epidemic of poliomyelitis. This plan includes an educational program stressing the need for early care and the essential teamwork of physician, nurse and physical therapist. She presents a preliminary report of results obtained in 87 cases under this plan. Fifty per cent of the patients returned to normal.

323. Moldaver, J.: Analysis of Neuromuscular Disorders in Poliomyelitis, *J. Bone & Joint Surg.* **26**:102-117 (Jan.) 1944.

324. McFarland, J. W., and Graves, D. A.: Poliomyelitis: Grading of Spasm in Infantile Paralysis, *Arch. Phys. Therapy* **25**:553-556 (Sept.) 1944.

325. Gurewitsch, A. D., and O'Neill, M. A.: Flexibility of Healthy Children, *Arch. Phys. Therapy* **25**:216-221 (April) 1944.

326. Hall, V. E.; Schamp, H. M.; Brown, C. E., and Davis, M. N.: Effect of Kenny Fomentation on the Strength of Voluntary Muscular Contracture in Man, *Arch. Phys. Therapy* **25**:96-99 (Feb.) 1944.

327. Stevenson, J. L.: Public Health Nursing in the 1943 Polio Epidemic, *Pub. Health Nursing* **36**:336-339 (July) 1944.

328. Draper, E.: An Emergency Plan in High Incidence Poliomyelitis, *Physiotherapy Rev.* **21**:96-99 (May-June) 1944.

319. Thompson, C. G.: Occupational Therapy and the Kenny Method, *Occup. Therapy* **22**:270-273 (Dec.) 1943.

320. Kabat, H., and Knapp, M. E.: The Mechanism of Muscle Spasm in Poliomyelitis, *J. Pediat.* **24**:123-137 (Feb.) 1944.

321. Bouman, H. D., and Schwartz, R. P.: The Degree, the Extent and the Mechanism of Muscle Spasm in Infantile Paralysis, *New York State J. Med.* **44**:147-153 (Jan. 15) 1944.

322. Schwartz, R. P.; Bouman, H. D., and Smith, W. K.: The Significance of Muscle Spasm, *J. A. M. A.* **126**:695-702 (Nov. 11) 1944.

occupation; 14 per cent obtained good results but have not yet returned to normal activity; 14 per cent obtained fair results, with no complete paralysis but with definite weakness, and 22 per cent had a residual definite loss of one or more muscle groups.

Poehler<sup>329</sup> outlines an ideal set-up for the treatment of poliomyelitis following the remodeling of "Sheltering Arms" in Minneapolis. She stresses the fact that patients during the convalescent stage of poliomyelitis are not sick in

329. Poehler, J. A.: Remodeled for "Polio" Patients, *Mod. Hosp.* 62:58-60 (Jan.) 1944.

## NII. NEUROMUSCULAR DISORDERS EXCLUSIVE OF POLIOMYELITIS

PREPARED BY WINTHROP M. PHELPS, M.D., BALTIMORE

During 1943 there was an increase in the volume of literature dealing with neuromuscular disorders. This is especially interesting in view of the pronounced decrease of the year before. The distribution of the material has changed only slightly. That referring to cerebral palsy has increased the most, and the articles on peripheral paralysis and surgery are close seconds. The papers dealing with pure research in the field are still scarce.

The material can be considered under nine chief headings, which are as follows: (1) cerebral palsy, (2) peripheral paralysis, (3) myopathies, (4) ataxia, (5) neuralgia, (6) diagnostic procedures, (7) surgery, (8) vitamins and (9) drugs.

*Cerebral Palsy.*—A paper by Lucksch<sup>331</sup> describes 2 cases, brought to autopsy, of the disease previously called "cerebral infantile paralysis." Lucksch suggests that the designation be changed to "encephalopathia infantum." The change, he feels, is more descriptive of conditions observed and yet is not specifically a description of a disease entity. [ED. NOTE.—This is an anatomic title whereas the usual term "cerebral palsy" is a descriptive one, and the latter, of course, is much more in keeping with American custom.]

Yannet<sup>332</sup> has written an interesting paper on the study of 86 patients with cerebral palsy. He notes that the average age of the mother at the time of birth of the affected child is greater than that found in the general population. The affected children tend to have a later ordinal

331. Lucksch, F.: Description of Two Autopsy Cases of "Cerebral Infantile Paralysis," with Suggestion for Changing Designation to "Encephalopathia Infantum," *Psychiat.-neurol. Wchnschr.* 45:137 (May 22) 1943.

332. Yannet, H.: Etiology of Congenital Palsy: Statistical and Clinical Study, *J. Pediat.* 24:38-45 (Jan.) 1944.

the sense that the word is usually understood and should not be treated in hospitals planned and maintained for acutely ill persons.

Gudakunst<sup>330</sup> discusses the problem of infantile paralysis, setting forth the gains made in the handling and treatment of patients. He brings out the purpose and scope of the work of The National Foundation for Infantile Paralysis, Inc.

330. Gudakunst, D. W.: Fighting Infantile Paralysis, *Survey* 80:254-256 (Sept.) 1944; Facing the Future in the Fight Against Infantile Paralysis, *J. Health & Phys. Educ.* 15:258 (May) 1944.

birth rank than would be normally expected. [ED. NOTE.—This might be expected in view of the recent observations in regard to the Rh factor.] He also finds that the incidence of mental deficiency in the nonaffected siblings is greater than would be expected from random selection. He finds an unusually high incidence of associated physical defects, especially those involving the eyes. [ED. NOTE.—In my experience, this is also true of hearing defects.] Yannet feels that this points to the importance of developmental cerebral malformations in the causation of cerebral palsy.

Phelps<sup>333</sup> describes the treatment of various types of cerebral palsy in some detail and emphasizes the need for proper classification of the individual cases in order to carry out differential treatment.

Salisbury<sup>334</sup> draws attention to the increased interest in cerebral palsy throughout the country and the greater number of cases encountered in the clinics and in private practice and emphasizes the great need for a national foundation for this condition, since it is as frequent in distribution as poliomyelitis.

Arieff and Kaplan<sup>335</sup> describe cerebellar ataxia associated with cerebral signs. This is, of course, not commonly seen, but it is well to bear in mind the complications of neurologic changes which may occur.

Welch and Kennard<sup>336</sup> describe flaccid paralysis in relation to the cerebral cortex. This is

333. Phelps, W. M.: Symposium on Orthopaedic Surgery: Treatment of Cerebral Palsies, *Clinics* 2:981-991 (Dec.) 1943.

334. Salisbury, P. A.: Needed—National Foundation for Cerebral Palsy, *Hospitals* 18:50-53 (April) 1944.

335. Arieff, A. J., and Kaplan, L. A.: Cerebellar Type of Ataxia Associated with Cerebral Signs, *J. Nerv. & Ment. Dis.* 100:135-141 (Aug.) 1944.

(Footnotes continued on next page)

important and was described some years ago by other investigators, in both the experimental and the clinical fields. The combination of spastic and flaccid paralysis does occur in many instances and is of cortical origin.

Thiébaud<sup>337</sup> describes spastic paralysis associated with xanthomas of tendons and describes the relationship of this syndrome to cerebrospinal cholesterinosis. The cerebral changes are important to bear in mind in any cases of xanthoma.

A number of articles have appeared this year on various types of treatment of the cerebral palsies.

Sidler<sup>338</sup> speaks of the general plan of therapy for children and goes into some detail with regard to methods.

Frank<sup>339</sup> writes concerning the advantages and the usefulness of occupational therapy for children with cerebral palsy, and Mason<sup>340</sup> describes speech rehabilitation in such cases.

Teza<sup>341</sup> writes concerning the motor reeducation in these cases as it is being carried out in Argentina.

*Peripheral Paralysis.*—Chavany<sup>342</sup> describes a post-traumatic neurologic syndrome with increasing atrophy and fibrillary contractions, which is of interest because of its traumatic origin.

Denny-Brown and Brenner<sup>343</sup> discuss paralysis produced by pressure and tourniquets in an article on the subject, with much more careful experimentation. They conclude that there is great variation of the rate of impairment of induction with variations in pressure and that the relationship is an expression of corresponding relative degrees of ischemia and not direct consequence of pressure on nerve fibers. They

describe in detail the microscopic histologic changes which occur by various staining methods. They conclude that from the evidence presented atrophy of a paralyzed muscle appears to be prevented by anatomic connection with the motor neuron in the absence of nerve impulse.

Dunning<sup>344</sup> reports a case of injury to the peroneal nerve (with foot drop) due to crossing the legs and points out that this habit may cause injury to the nerve. [Ed. Note.—It does not seem as if the danger is especially great unless there is some other complication in the blood or the nerve supply, since this practice is certainly almost universal.]

Lewin<sup>345</sup> and Laird and Mueller<sup>346</sup> also consider peroneal paralysis but from different cause. The former considers that it is a definite pressure palsy (of the lateral popliteal nerve) in the paralyzed limb, while the latter authors describe it as a "bombardier's palsy."

Connell<sup>347</sup> describes a case of paralysis which appears to have resulted from the use of dinitro toluene. The patient was treated by rest in bed and made a gradual partial recovery. The author cites other cases of the same type which have been observed and which resulted in death.

MacKeith<sup>348</sup> describes paralysis of the extremities due to polyarthritis nodosa and Love and Horton<sup>349</sup> an ulnar paralysis due to arteriovenous fistula.

*Myopathies.*—Laha<sup>350</sup> considers the question of myatonia congenita (a subject on which little has been written in the last few years).

Shank, Gilder and Hoagland<sup>351</sup> review 40 cases of progressive dystrophy with regard to the changes that occur in various stages of the disease and the age distribution and the onset.

336. Welch, W. K., and Kennard, M. A.: Relation of Cerebral Cortex to Spasticity and Flaccidity, *J. Neurophysiol.* 7:255-268 (Sept.) 1944.

337. Thiébaud, F.: Spastic Paraplegia Associated with Xanthomas of Tendons: Relation of This Syndrome to Cerebrospinal Cholesterinosis, *Rev. neurol.* 74:313-315 (Nov.-Dec.) 1942.

338. Sidler, A.: Therapy of Spastic Paralysis in Children, *Praxis* 33:261-264 (April 20) 1944.

339. Frank, C.: Occupational Therapy for Children with Cerebral Palsy, *Occup. Therapy* 23:103-114 (June) 1944.

340. Mason, M. K.: Speech Rehabilitation, *Physiotherapy Rev.* 23:237-242 (Nov.-Dec.) 1943.

341. Teza, A.: Kinesitherapy of Little's Disease: Motor Education, *Arch. argent. de pediat.* 21:181-186 (Feb.) 1944.

342. Chavany, J. A.: Post-Traumatic Neurologic Syndrome: Extensively Progressive Amyotrophy with Secondary Paralysis and Fibrillary Contractions, *Presse méd.* 50:347 (May 10) 1942.

343. Denny-Brown, D., and Brenner, C.: Paralysis of Nerve Induced by Direct Pressure and by Tourniquet, *Arch. Neurol. & Psychiat.* 51:1-26 (Jan.) 1944.

344. Dunning, H. S.: Injury to Peroneal Nerve (with Foot Drop) Due to Crossing the Legs, *Arch. Neurol. & Psychiat.* 51:179-181 (Feb.) 1944.

345. Lewin, W.: Pressure Palsy (of Lateral Popliteal Nerve) in Paralyzed Limb, *Lancet* 2:756-758 (Dec. 18) 1943.

346. Laird, G. J., and Mueller, M. J.: Bombardier's Palsy, *Air Surgeon's Bull.* (no. 9) 1:19 (Sept.) 1944.

347. Connell, E. D.: Paralysis from Chemical Poisoning (Probably Dinitrotoluene): Case, *Memphis M. J.* 19:59-60 (April) 1944.

348. MacKeith, R.: Localized Subcutaneous Edema with Weakness of Limb Muscles: Syndrome Due to Polyarthritis Nodosa, *Brit. M. J.* 1:139-142 (Jan. 29) 1944.

349. Love, J. G., and Horton, B. T.: Paralysis of Ulnar Nerve Due to Arteriovenous Fistula, *Proc. Staff Meet., Mayo Clin.* 19:441-444 (Aug. 23) 1944.

350. Laha, P. N.: Amyotonia Congenita, with Illustrative Case Note, *J. Indian M. A.* 13:20-22 (Oct.) 1943.

351. Shank, R. E.; Gilder, H., and Hoagland, C. L.: Progressive Dystrophy: Clinical Review of Forty Cases, *Arch. Neurol. & Psychiat.* 52:431-442 (Dec.) 1944.

They discuss the previous methods of treatment, including amino acids, vitamins, glandular preparations and other agents. They report extensive studies of basal metabolic rates, tolerance tests, and other aspects of the disease. Their study of the distribution shows the definite hereditary nature of the condition.

Mackay<sup>352</sup> presents an interesting case of dystrophy and the status of treatment at the present time. The particular type which he describes is the Charcot-Marie-Tooth type.

Schwartz<sup>353</sup> also describes the various effects of progressive neuropathic (peroneal) muscular atrophy (Charcot-Marie-Tooth disease), pointing out the inheritance factors as well as the clinical observations.

*Ataxia.*—Brugsch and Hauptmann<sup>354</sup> describe an interesting combination of Friedreich's ataxia in combination with neuropathic (peroneal) muscular atrophy (Charcot-Marie-Tooth disease).

*Neuralgia.*—Doupe, Cullen and Chance<sup>355</sup> discuss the causalgic type of pain that is found in post-traumatic neuralgia.

*Diagnostic Procedures.*—There has been considerable work done in electromyographic study on the various forms of nerve-muscle disturbances in the last few years.

Brazier, Watkins and Schwab<sup>356</sup> illustrate the difference in various types of polyneuritis and poliomyelitis with regard to electromyographic records.

Hoefer and Guttman<sup>357</sup> have made extensive electromyographic studies to determine the level of spinal cord lesions. They present the results in 24 cases and conclude that motor unit discharges recorded from the relaxed muscles may indicate the level of a lesion of the spinal cord, even in the absence of clinical manifestations suggestive of involvement of the anterior horn

cells or motor roots. In 17 of 24 cases the lesion was satisfactorily localized, and in the others fairly close localization was obtained; false localization was obtained in only 2 cases.

De Jong<sup>358</sup> has devised an instrument for electrical examination and treatment of peripheral nerves, which is a small light unit and accomplishes many purposes by virtue of features usually not combined in a single instrument.

Pollock and others<sup>359</sup> have studied denervated muscles with various amperages of current and noted the changes which occur when regeneration is taking place.

Licht<sup>360</sup> has formulated an outline of electrodiagnosis of neuromuscular disease for the army.

*Surgery.*—Cerebral Palsy: Chandler<sup>361</sup> described the surgical procedures which are in present use for correcting deformities of spastic paralysis and the indications for and the various results obtained by the different operations.

Peripheral Nerve: Schulze<sup>362</sup> has described a method of operation for correcting the deformities due to paralysis of the trapezius muscle.

Huguier and Nardi<sup>363</sup> have corrected the paralysis of the arm due to stretching of the brachial plexus by an injury. They have carried out this by a combination of arthrodesis of the shoulder and wrist and transplantation of the tendon. The results have been satisfactory function in the arm for considerable usefulness.

Weiss<sup>364</sup> has devised technics for the union of severed nerves without sutures, by the use of tantalum cuffs.

352. Mackay, R. P.: Progressive Muscular Dystrophy. Proc. Interst. Postgrad. M. A. North America (1943), 1944, pp. 88-91.

353. Schwartz, L. A.: Clinical, Histopathologic and Inheritance Factors in Peroneal Muscular Atrophy (Charcot-Marie-Tooth Type), J. Michigan M. Soc. 43: 219-230 (March) 1944.

354. Brugsch, H. G., and Hauptmann, A.: Familial Occurrence of Friedreich's Ataxia with Charcot-Marie-Tooth Neural Muscular Atrophy, Bull. New England M. Center 6:42-48 (Feb.) 1944.

355. Doupe, J.; Cullen, C. H., and Chance, G. Q.: Post-Traumatic Pain and Causalgic Syndrome, J. Neurol., Neurosurg. & Psychiat. 7:33-48 (Jan.-April) 1944.

356. Brazier, M. A. B.; Watkins, A. L., and Schwab, R. S.: Electromyographic Studies of Muscle Dysfunction in Infectious Polyneuritis and Poliomyelitis, New England J. Med. 230:185-189 (Feb. 17) 1944.

357. Hoefer, P. F. A., and Guttman, S. A.: Electromyography as Method for Determination of Level of Lesions in Spinal Cord, Arch. Neurol. & Psychiat. 51: 415-422 (May) 1944.

358. de Jong, H.: Simplification of Method of Electrical Examination and Therapy of Nerves and Muscles. North Carolina M. J. 5:91-92 (March) 1944.

359. Pollock, L. J., and others: Electrodiagnosis by Means of Progressive Currents of Long Duration: Studies on Cats with Experimentally Produced Section of Sciatic Nerves, Arch. Neurol. & Psychiat. 51:147-154 (Feb.) 1944.

360. Licht, S.: Neuromuscular Electrodiagnosis: Outline, Bull. U. S. Army M. Dept., January 1944, no. 72, pp. 74-80.

361. Chandler, F. A.: Surgical Procedures Commonly Used in Correcting Deformities of Spastic Paralysis, Clinics 2:992-1001 (Dec.) 1943.

362. Schulze, R.: Trapezius Paralysis: Surgical Therapy, Zentralbl. f. Chir. 70:692 (May 8) 1943.

363. Huguier, J., and Nardi: Complete Impotence of Arm Due to Traumatic Elongation of Brachial Plexus: Arthrodesis of Shoulder and of Wrist with Tendon Transplants; Satisfactory Functional Result, Mém. Acad. de chir. 68:168-173 (Feb. 11-March 4) 1942.

364. Weiss, P.: Sutureless Reunion of Severed Nerves with Elastic Cuffs of Tantalum, J. Neurosurg. 1:219-225 (May) 1944; Technology of Regeneration: Review; Sutureless Tubulation and Related Methods of Nerve Repair, ibid. 1:400-450 (Nov.) 1944.

Young<sup>365</sup> points out the advisability of as early suturing as possible and the effects of delay.

Thomsen<sup>366</sup> and Thomsen, Altamirano and Luco<sup>367</sup> have discussed the effects of tenotomy on muscle contractures and neuromuscular transmission.

Blalock<sup>368</sup> reports favorable results in the treatment of myasthenia gravis by thymectomy.

*Vitamins.*—The work with vitamins has become less and less significant in the last two years with regard to their effects on neuromotor pathologic changes in general. There are, of course, exceptions to this, but these changes occur apparently only in the presence of severe avitaminosis, and it appears that relative avitaminosis is not of so much importance.

Hines, Lazere and Thomson<sup>369</sup> described the effects of different intakes of vitamins of the B complex on neuromuscular regeneration and found that it was not affected by withdrawal of the vitamins and that excess intakes caused no enhancement of regeneration.

Hines, Lazere and Thomson<sup>370</sup> discuss a similar study with regard to the effects of vitamin C on neuromuscular regeneration in guinea pigs. They conclude that the regenerating muscles of animals subsisting on low intakes of ascorbic acid were weaker than those with a sufficient quantity but that excess intakes of ascorbic acid had no beneficial effect.

Minot and Frank<sup>371</sup> confirmed previous writers in the fact that vitamin E therapy is not noticeably effective against pseudohypertrophy.

365. Young, J. Z.: Effect of Delay on Success of Suture, *Proc. Roy. Soc. Med.* **37**:551-552 (Aug.) 1944.

366. Thomsen, P.: Recuperation from Effects of Tenotomy on Neuromuscular Transmission, *Rev. de med. y aliment.* **5**:312 (April-July) 1943.

367. Thomsen, P.; Altamirano, M., and Luco, J. V.: Effects of Tenotomy on Neuromuscular Transmission, *Rev. de med. y aliment.* **5**:84 (Oct.-Jan.) 1941-1942.

368. Blalock, A.: Thymectomy in Treatment of Myasthenia Gravis: Twenty Cases, *J. Thoracic Surg.* **13**:316-339 (Aug.) 1944.

369. Hines, H. M.; Lazere, B., and Thomson, J. D.: Effects of Different Intakes of B-Complex Vitamins upon Neuromuscular Regeneration, *Proc. Soc. Exper. Biol. & Med.* **55**:97-98 (Feb.) 1944.

370. Hines, H. M.; Lazere, B.; Thomson, J. D., and Cretzmeyer, C. H.: Study of Neuromuscular Regeneration Under Different Levels of Vitamin C Intake, *J. Nutrition* **27**:303-308 (April) 1944.

371. Minot, A. S., and Frank, H. E.: Serum Tocopherol: Relation of Failure of Vitamin E Therapy

Mims<sup>372</sup> discusses the same question for the myopathies, with a conclusion that there is little if any value in use of vitamin E for these conditions.

*Drugs.*—The use of drugs for neuromotor conditions has increased considerably in the last year or two, and articles about their use are beginning to appear with greater frequency. The effects of curare and its synthetic derivatives are being widely tested, but as yet few articles concerning this have appeared in the literature.

Chiodin<sup>373</sup> describes the effect of curare and erysopine in the treatment of spastic paralysis with some evidence of improvement in certain of these conditions.

Schaubel<sup>374</sup> discusses neostigmine as an adjunct in the treatment of cerebral palsy and not definite improvement in some of the patients especially in the field of their speech.

Oppikofer<sup>375</sup> discusses the use of neostigmine in treatment of myasthenia gravis and points out the effectiveness of this drug.

Hoagland, Shank and Gilder<sup>376</sup> discuss the effect of testosterone propionate on creatinuria in progressive atrophy and dystrophy. They feel that if excretion of creatinine which occurs after testosterone medication may be regarded as a true storage phenomenon, it would justify the administration of this hormone over a prolonged period to see whether muscle function could be improved thereby. Their report is preliminary one at the present time.

for Pseudohypertrophic Dystrophy, *Am. J. Dis. Child* **67**:371-375 (May) 1944.

372. Mims, W. D.: Value, if Any, of Vitamin E in Myopathies, with Case Reports, *Memphis M. J.* **19**:135-136 (Sept.) 1944.

373. Chiodin, L.: Curarizing Therapy in Disorders of Children: Effect of Erysopine (Alkaloid of Erythrina) and Curare, *Rev. Soc. pediatri. de Rosario* **8**:139-151 (May-Aug.) 1943.

374. Schaubel, H. J.: Prostigmine (Neostigmine) as Adjunct in Treatment of Cerebral Palsy, *Physiotherapy Rev.* **24**:236-237 (Nov.-Dec.) 1944.

375. Oppikofer, E. K.: Disorders of Speech and Deglutition in Myasthenia Gravis Pseudoparalysis: Value of Neostigmine Therapy, *Pract. oto-rhino-laryng.* **5**:238-249, 1943.

376. Hoagland, C. L.; Shank, R. E., and Gilder, H.: Effect of Testosterone Propionate and Methyl Testosterone (Androgens) on Creatinuria in Progressive Dystrophy, *Proc. Soc. Exper. Biol. & Med.* **55**:49-51 (Jan.) 1944.

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